IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

IN RE PLAVIX® MARKETING, SALES PRACTICE AND PRODUCTS LIABILITY LITIGATION (NO. II)	MDL DOCKET NO. 2418
UNITED STATES OF AMERICA, ET AL. *ex rel.* JKJ PARTNERSHIP 2011 LLP, *Plaintiffs*, v. SANOFI-AVENTIS U.S. LLC; SANOFI-AVENTIS U.S. SERVICES INC.; AVENTIS INC.; AVENTIS PHARMACEUTICALS, INC.; BRISTOL-MYERS SQUIBB COMPANY; and BRISTOL-MYERS SQUIBB SANOFI PHARMACEUTICALS HOLDING PARTNERSHIP, *Defendants*.	CASE No.: 3:11-cv-6476-FLW-LHG **SECOND AMENDED COMPLAINT FOR VIOLATIONS OF THE FEDERAL FALSE CLAIMS ACT AND STATE LAW COUNTERPARTS** **JURY TRIAL DEMANDED**

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SECOND AMENDED COMPLAINT FOR FALSE CLAIMS ACT VIOLATIONS UNDER 31 U.S.C. § 3729 *ET SEQ.* AND STATE LAW COUNTERPARTS

This is a *qui tam* action brought on behalf of the United States of America, and numerous State Governments, by JKJ PARTNERSHIP 2011 LLP ("Relator"), by and through its attorneys, against Defendants Sanofi-Aventis U.S. LLC, Sanofi-Aventis U.S. Services Inc., Aventis Inc., Aventis Pharmaceuticals Inc., Bristol-Myers Squibb Company, and Bristol-Myers Squibb Sanofi Pharmaceuticals Holding Partnership, pursuant to the Federal Civil False Claims Act, 31 U.S.C. § 3729, *et seq.* and analogous State False Claims Acts.[1]

INTRODUCTION

1. Relator seeks to recover damages and civil penalties, from at least 2005 through 2013, arising from false or fraudulent claims paid by the United States and the *Qui Tam* States for

[1] **California** False Claims Act, Cal. Gov't Code § 12650 *et seq.* (first eff. Jan. 1, 1988); **Colorado** Medicaid False Claims Act, Colo. Rev. Stat. § 25.5-4-304 *et seq.* (first eff. July 1, 2006); **Connecticut** False Claims Act, Conn. Gen. Stat. § 17b-301a *et seq.* (first eff. Oct. 5, 2009); **Delaware** False Claims and Reporting Act, Del. Code Ann. tit. 6, § 1201 *et seq.* (first eff. June 30, 2000); **District of Columbia** False Claims Act, D.C. Code § 2-308.13 *et seq.* (first eff. Feb. 21, 1986); **Florida** False Claims Act, Fla. Stat. § 68.081 *et seq.* (first eff. July 1, 1994); **Georgia** False Medicaid Claims Act, Ga. Code Ann. § 49-4-168 *et seq.* (first. eff. May 24, 2007); the **Illinois** False Claims Whistleblower Reward and Protection Act, 740 Ill. Comp. Stat. § 175/1 *et seq.* (first eff. Jan. 1, 1992); **Indiana** False Claims and Whistleblower Protection Act, Ind. Code § 5-11-5.5 *et seq.* (first eff. July 1, 2005); the **Iowa** False Claims Act, Iowa Code § 685.1 *et seq*. (first eff. July 1, 2010); **Louisiana** Medical Assistance Programs Integrity Law, La. Rev. Stat. Ann. § 46:439.1 *et seq.* (first eff. 1997); the Massachusetts False Claims Act, Mass. Gen. Laws ch. 12, § 5A *et seq.* (first eff. 2000); **Michigan** Medicaid False Claims Act, Mich. Comp. Laws § 400.601 *et seq.* (first eff. 2005); **Minnesota** False Claims Act, Minn. Stat. § 15C.01 *et seq.* (first eff. July 1, 2010); **Montana** False Claims Act, Mont. Code Ann. § 17-8-401 *et seq.* (first eff. Oct. 1, 2005); **Nevada** False Claims Act, Nev. Rev. Stat. § 357.010 *et seq.* (first eff. 1999); **New Jersey** False Claims Act, N.J. Stat. Ann. § 2A:32C-1 *et seq.* (first eff. Apr. 15, 2008); **New York** False Claims Act, N.Y. State Fin. Law § 187 *et seq.* (first eff. Apr. 1, 2007); **North Carolina** False Claims Act, N.C. Gen. Stat. § 1-605 *et seq.* (first eff. Jan. 1, 2010); **Oklahoma** Medicaid False Claims Act, Okla. Stat. tit. 63, § 5053 *et seq.* (first eff. Nov. 1, 2007); **Rhode Island** False Claims Act, R.I. Gen. Laws § 9-1.1-1 *et seq.* (first eff. Feb. 15, 2008); **Tennessee** Medicaid False Claims Act, Tenn. Code Ann. § 71-5-181 *et seq.* (first eff. 1993) and/or and Tennessee False Claims Act, Tenn. Code Ann. § 4-18-101 *et seq.*; **Virginia** Fraud Against Taxpayers Act, Va. Code Ann. § 8.01-216.1 *et seq.* (first eff. Jan. 1, 2003); **Washington** Medicaid False Claims Act, Wash. Rev. Code § 74.66.005 *et seq.* ((first eff. Sept. 5, 2012); and **Wisconsin** False Claims for Medical Assistance Law, Wis. Stat. § 20.931 *et seq.* (first eff. Oct. 27, 2007, repealed from and after July 14, 2015) (collectively the "State *Qui Tam* statutes" or "*Qui Tam* States").

the antiplatelet drug Plavix, which Defendants promoted as *the* standard of care for *all* antiplatelet and antithrombotic patients—including patients who received stents—notwithstanding their knowledge that the drug had little or no effect, and was therefore medically contraindicated, for over 30% of patients.

2. As early as [redacted], Defendants knew, but concealed the fact that their blockbuster drug Plavix had no demonstrable pharmacodynamic effect for many patients who had been prescribed the drug. They also knew that these "non-responders" or "low responders" were not entirely genetically random. Individuals whose ethnic background was African-American or Asian-American had a much higher risk of non-response to Plavix than other ethnicities—a fact which would have made it possible to alert physicians to monitor these patients more closely or choose a different medical or surgical course of treatment. When Defendants learned of this risk (inherent in over 30% of Plavix "non-responders" or "low responders"), they [redacted].[2] Defendants referred to this as the Plavix "Variability of Response" (or "VOR") issue. Rather than change the label to provide "adequate instructions" for Plavix's safe and effective use, or alert the medical community and Government Programs that their drug was ineffective for these patients, Defendants chose a strategy to "[redacted]"[3] so they could continue to "Expand & Protect" Plavix profits—even if it meant jeopardizing the health of millions of Americans and bilking Government Programs out of billions of dollars.

3. The linchpin of Defendants' strategy was a calculated scheme to conceal or marginalize adverse Plavix research studies, thereby causing physicians to unwittingly prescribe an ineffective treatment for those patients and depriving them of other potentially more effective

[2] [redacted]

[3] [redacted]

treatment options. Defendants deployed this strategy through corporate influence that permeated every aspect of Plavix clinical research, including: the choice of researcher (favoring only those they could control); study design (including the trial population, doses, duration of the trial, and the outcome and safety measures to be tracked); control of the data and data analysis; ghost-writing the manuscripts for articles; publication decisions; and publicity following publication. Most important, Defendants made it a policy to refuse funding for any research that proposed to examine the non-responder issue, from the outset viewing these studies as bearing "[redacted]" or as "[redacted]" because they would be "[redacted]" to Plavix sales. Their strategy was, as one employee put it, to "[redacted]."[4]

4. When smaller, privately-funded VOR studies (with the efforts of Dr. Paul A. Gurbel and others) first reported the VOR issue in 2001, Defendants engaged in an elaborate campaign to obfuscate and counter this research, including through a network of "Key Opinion Leaders" ("KOLs") who would insist that, to the extent there was any problem, it was minor and that there was no evidence correlating Plavix non-response to adverse clinical outcomes.

5. From the start, Defendants promoted Plavix to physicians (through their sales representatives) and to patients (through direct-to-consumer advertising) as safe and effective for *all* patients who needed an antithrombotic or antiplatelet medication. Even as evidence began to appear that Asian-American and African-American patients could be at the greatest risk to be Plavix non-responders, Defendants initiated what they called a Plavix "Living Proof" campaign that featured photos of actors portraying these very same ethnic groups as the most appropriate patients for treatment. Although they knew non-responders would have much reduced (or no) therapeutic benefit, Defendants' rallying cry remained that Plavix should be used to treat *every*

[4] [redacted].

patient who needed an antiplatelet or antithrombotic agent: "[redacted]"[5]

6. Data shows that, in the 30+% of patients who are Plavix non-responders, the most common adverse effect of being placed on Plavix is a coronary thrombosis—which often results in death. Yet, when adverse event reports were made to the FDA through MedWatch showing that Plavix had been ineffective for its intended use—including numerous reports that patients taking the drug had no (or much reduced) platelet inhibition, often following a heart attack or stroke—Defendants did nothing to notify physicians or patients of this risk.

7. After years of Defendants avoiding their obligation to ensure the Plavix label provided adequate instructions to physicians for its safe and effective use, or to otherwise inform the medical community, in 2010 the FDA required Defendants to add a "Black Box Warning" to the Plavix package insert, finally notifying doctors and patients that there was a risk associated with "poor metabolizers" for whom the drug might be ineffective. But, even then, with competition appearing from other brand drugs (and with generic versions of Plavix soon to appear), Defendants flouted the Black Box Warning by continuing with the same marketing strategy—advising physicians and patients that Plavix was appropriate for *all* patients who needed antiplatelet or antithrombotic therapy, all the while improperly diminishing the non-responder risk.

8. For years Defendants had regularly trained their sales forces about the non-responder research, instructing them never to proactively inform physicians of this issue. If a physician were to raise any VOR concerns, sales representatives were taught to provide a message that sidestepped the issue as only a minor one on which there was no correlation to clinical outcomes and impacting only a small minority of patients. Even after the FDA required the label

[5] [redacted]

change to inform physicians and patients of the VOR risk, rather than provide meaningful guidance to the medical community about how to treat these patients, Defendants engaged in a cynical campaign to diminish the problem as only impacting very few patients, instead urging doctors that they could treat these patients by simply doubling the loading dose of Plavix. Not only was there no adequate clinical evidence supporting the claim to double the loading dose, for many of these patients doubling the loading dose caused dangerous (even fatal) bleeding risks associated with Plavix.

9. Throughout, Defendants have denied [redacted] *i.e.*, that Plavix had much reduced (or no) effect for many patients. Defendants instead deceptively claimed that reports of decreased efficacy could be the product of patient error (*e.g.*, failing to take the medication) or physician error (*e.g.*, prescribing an inadequate dosage regimen).

10. Billions of dollars' worth of Plavix prescriptions have been submitted to and paid by Government Programs such as Medicare, Medicaid, the Federal Employee Health Benefit Program, and State health benefit programs (collectively "Government Programs"). All the while Defendants knew, and concealed from the Government Programs, that for over 30% of patients Plavix had little to no pharmacodynamic effect and thus added nothing to improve the patients' outcomes.

11. Moreover, Government Purchasers, such as the United States Department of Veterans Affairs and the Department of Defense, as well as numerous States, entered into purchase agreements directly with Defendants, and/or indirectly through drug wholesalers, to purchase what Defendants had represented was a safe and effective lifesaving drug that worked for its intended

purpose for *all* patients, and therefore was suitable for all Government Program beneficiaries. These representations were materially false.

12. Defendants' illegal promotion of Plavix has caused hundreds of thousands of contraindicated, and therefore medically unnecessary and unreasonable, prescriptions to be submitted to Government Programs throughout the United States. Defendants' misconduct cheated the Government Programs out of billions of dollars that should not have been paid, thereby illegally enriching Defendants at taxpayer expense and subjecting patients to unapproved, ineffective and unsafe uses of Plavix.

13. Defendants' concealment and deception caused physicians to write, and Government Programs to reimburse, as well as Government Purchasers to purchase, contraindicated, and therefore medically unnecessary and unreasonable, Plavix prescriptions for millions of patients that Defendants' [redacted] would be predisposed to experience greatly diminished or no responsiveness to Plavix, rendering it little more than a placebo and placing those patients at significant risk.

14. At all relevant times, Defendants knew that Plavix was being purchased by Government Purchasers (including the Department of Veterans Affairs and the Department of Defense) or reimbursed by Government Programs.

15. Defendants knew that their illegal conduct would lead to the submission of false statements and/or false or fraudulent claims to Government Purchasers and Government Programs. But for Defendants' illegal conduct, not only would those contraindicated, and therefore medically unnecessary and unreasonable, prescriptions not have been written, but Government Purchasers would not have entered into the contracts, directly and/or indirectly, with Defendants for the purchase of tens of millions of doses of Plavix. As a result, Defendants have caused the submission

of false statements, and/or false or fraudulent claims, to Government Purchasers and Government Programs, from which Defendants have received billions of dollars.

II. JURISDICTION AND VENUE

16. This Court has subject matter jurisdiction pursuant to 31 U.S.C. § 3732(a), 28 U.S.C. § 1331, and 28 U.S.C. § 1345.

17. The Court has original jurisdiction of the State law claims pursuant to 28 U.S.C. § 1367 and 31 U.S.C. § 3732(b), because this action is brought under the laws of the respective States for the recovery of funds paid by the *Qui Tam* States, and it arises from the same transactions or occurrences brought on behalf of the United States under 31 U.S.C. § 3730.

18. This Court has personal jurisdiction over Defendants because, among other things, Defendants transact business in this judicial district and engaged in wrongdoing in this judicial district.

19. Venue is proper in this judicial district under 31 U.S.C. § 3732(a) and 28 U.S.C. § 1391(b)-(c). Defendants transact business within this judicial district, and acts proscribed by 31 U.S.C. § 3729 occurred in this judicial district.

20. The causes of action alleged herein are timely brought because, among other things, of efforts by Defendants to conceal from the United States and the States their wrongdoing in connection with the allegations made herein.

21. This Complaint was properly filed in camera and under seal, as required by 31 U.S.C. § 3730(b)(2) and the various State FCAs, and remained under seal for at least sixty days as required by the FCA. Pursuant to 31 U.S.C. § 3730(b)(2), the Government may elect to intervene and proceed with the action within sixty days after it receives both the complaint and the evidence submitted to it, or while the case otherwise remains under seal. Pursuant to 31 U.S.C. § 3730(c)(3),

upon a showing of good cause the Government may also intervene after the case is unsealed and while the Relator is prosecuting the case.

22. Contemporaneous with the filing of the original Complaint, Relator properly served a copy of the Complaint and written disclosure of substantially all material evidence and information upon the United States and the Plaintiff States, as required by 31 U.S.C. § 3730(b)(2) and the similar provisions of each State FCA.

23. Relator is not aware of any "public disclosure," as that term is used in the Federal FCA, 31 U.S.C. § 3730(e)(4)(A), and/or the State FCAs, of the allegations forming the core elements of the Counts against Defendants.

24. Moreover, in the event there is found to have been any such public disclosure, Relator is the "original source," as that term is used in the Federal FCA, 31 U.S.C. § 3730(e)(4)(B), and/or the State FCAs, of the allegations or transactions forming the core elements of the Counts against Defendants. Relator had "direct and independent knowledge of the information on which the allegations are based" through direct business relationships with Defendants, and "voluntarily provided the information to the Government before filing" this action. Furthermore, and consistent with the meaning of "original source" under the Federal FCA on and after March 23, 2010, Relator either: "voluntarily disclosed to the Government the information on which allegations or transactions in a claim are based" prior to any public disclosure under subsection (e)(4)(A); or has "knowledge that is independent of and materially adds to the publicly disclosed allegations or transactions and voluntarily provided the information to the Government before filing" this action.

25. The United States and the States have reviewed the allegations in the Second Amended Complaint and have declined to intervene.

III. PARTIES

A. PLAINTIFF/RELATOR JKJ PARTNERSHIP 2011 LLP

26. Plaintiff/Relator, a Delaware limited liability partnership, is named JKJ PARTNERSHIP 2011 LLP (Registered Office: 3500 S. DuPont Highway, Dover, DE 19901). There are three JKJ partners: Paul A. Gurbel, M.D., Jeffrey A. Stahl, M.D., and Kelly D. Evans.

27. Pursuant to Section 15-201(a) of the Delaware Revised Uniform Partnership Act, JKJ PARTNERSHIP 2011 LLP ("JKJ Partnership") is not distinct from its partners, who have personal knowledge of the aforesaid false claims, statements, concealments, and receipts.

28. Paul A. Gurbel, M.D. earned his medical degree at the University of Maryland School of Medicine and completed an internship and residency in internal medicine at Duke University Medical Center in Durham, North Carolina. Dr. Gurbel then completed a fellowship in pulmonary and critical care medicine at Johns Hopkins University, followed by fellowships in cardiovascular disease and interventional cardiology as well as a chief residency in internal medicine at Duke. He is board certified in internal medicine, cardiovascular disease, and interventional cardiology by the American Board of Internal Medicine. In addition to prolific research, Dr. Gurbel remains one of the busiest cardiac interventionalists on the east coast. In 2011, Dr. Gurbel was recognized by the US NEWS WORLD REPORT, THE WASHINGTON POST MAGAZINE, BALTIMORE MAGAZINE and other agencies as being one of the "best physicians" in America. Dr. Gurbel serves on the editorial boards for several journals, including JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY, THE AMERICAN HEART JOURNAL, JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY HEART FAILURE, THE JOURNAL OF THE ROYAL SOCIETY OF MEDICINE, and on the Scientific Session Committee for Transcatheter Cardiovascular Therapeutics and the International Scientific Advisory Board, International Society of Thrombosis and Haemostasis. In addition to book chapters and monographs, he has authored nearly 400 major articles in peer-

reviewed journals, most recently including JAMA, CIRCULATION, JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY, DIABETES, AMERICAN JOURNAL OF CARDIOLOGY, AMERICAN HEART JOURNAL, THROMBOSIS AND HAEMOSTASIS, JOURNAL OF THROMBOSIS AND HAEMOSTASIS, PLATELETS, JOURNAL OF INTERVENTIONAL CARDIOLOGY, LANCET and NATURE. His research and concepts have been published in over 1000 peer-reviewed documents. In 2012 he authored 30 manuscripts in the peer-reviewed literature. In 2012, three peer-reviewed papers developed by Dr. Gurbel and his team were named "Most Important Papers in Antiplatelet Therapy" by CIRCULATION. The breakthrough findings of Dr. Gurbel and his team have influenced guidelines related to antithrombotic and antiplatelet therapy reported by the American Heart Association (AHA), the American College of Cardiology (ACC), and the European Society of Cardiology (ESC). Their research has also created a platform for the discovery of new antithrombotic drugs.

29. Jeffrey A. Stahl, M.D. is a practicing cardiologist (heart specialist) in Manhasset, New York. He graduated with honors from Albert Einstein College of Medicine of Yeshiva University in 1984, completed his residency in Internal Medicine at Bronx Municipal Hospital Center, and then completed a Cardiovascular Disease Fellowship at The Mt. Sinai Medical Center in Manhattan. Dr. Stahl later served as Director of Non-Invasive Cardiology for eight years at St. Francis Hospital, The Heart Center, in Roslyn, New York. Dr. Stahl has been affiliated with St. Francis Hospital for the past twenty-four years as a consultant and attending cardiology physician. He has also been an Assistant Professor of Medicine at NYU Langone Medical Center for the past decade. He is board certified in Cardiovascular Disease and Internal Medicine.

30. Kelly D. Evans is an award-winning Specialty Sales Representative with experience in cardiology (interventional, cardiac, thoracic), oncology, hematology, nephrology, neurology, infectious disease, general surgery, dermatology, orthopedics, pediatrics, internal

medicine, podiatry, rheumatology, pain management, endocrinology, gynecology, urology, and veterinary medicine. Ms. Evans worked as a sales representative at Sanofi-Aventis Pharmaceuticals from 2006 through 2010, serving as a Specialty Sales Professional (2006-2008), Hospital Representative/Cardiovascular (2008-2010), and as a Medical Center Representative Certified Hospital Field Trainer (2008-2010). She sold Plavix on behalf of Sanofi-Aventis.

B. THE SANOFI-AVENTIS DEFENDANTS

31. Defendant Sanofi-Aventis U.S. LLC is a Delaware limited liability company with headquarters and research facilities located at 55 Corporate Drive, Bridgewater, New Jersey 08807, and is a subsidiary of Defendant Aventis Inc.

32. Defendant Sanofi-Aventis U.S. Services Inc. (f/k/a Sanofi-Aventis U.S. Inc.) is a Delaware corporation with offices located at 55 Corporate Drive, Bridgewater, New Jersey 08807.

33. Defendant Aventis Pharmaceuticals Inc. is a Delaware corporation with offices located at 300 Somerset Corporate Boulevard, Bridgewater, New Jersey 08807.

34. Defendant Aventis Inc. is a Pennsylvania corporation with offices located at 3711 Kennett Pike, Greenville, Delaware 19807, and is the parent company of Defendant Sanofi-Aventis U.S. LLC.

35. Defendants Sanofi-Aventis U.S. LLC, Sanofi-Aventis U.S. Services Inc., Aventis Inc. and Aventis Pharmaceuticals Inc. (collectively referred to herein as "Sanofi" or the "Sanofi Defendants") are wholly-owned U.S. subsidiaries of Sanofi-Aventis—a holding company of a consolidated group of subsidiaries that engage in research and development, manufacturing, and marketing of pharmaceutical products for sale principally in the prescription market. The U.S. headquarters of Sanofi-Aventis, and the location from which its U.S. activities are directed, is 55 Corporate Drive, Bridgewater, New Jersey 08807. Among the products marketed and sold by

Sanofi-Aventis throughout the United States, including within this judicial district, is the antiplatelet drug Plavix.

36. A substantial percentage of Plavix sold in the United States was paid or reimbursed by various Government Purchasers and Government Programs, including health benefit carriers offering benefits under the Federal Employees Health Benefits Program ("FEHBP") under a prime contract with the Blue Cross Blue Association, the Health Insurance Program for the Elderly and Disabled, more commonly referred to as the Medicare Program, 42 U.S.C. § 1395, *et seq*., via Medicare Part C (also known as Medicare+Choice), Medicare Part B, Medicare Advantage, Medicare Part D, the Indian Health Service, Medicaid, the Mail Handler's Health Benefit Plan, the U.S. Secret Service Employees Health Association Health Benefit Plan, the Civilian Health and Medical Program of the Uniformed Services ("CHAMPUS," now known as "TRICARE") and the Veteran's Health Administration ("VHA"), as well as various State health benefit plans (collectively, the "Government Programs").

37. Sanofi publicly holds itself out as a company committed to high ethical standards, as well as being in compliance with fraud, waste and abuse laws enacted to prevent fraud, over-utilization, over-billing, and safeguard the health and safety of Government Program beneficiaries. *See generally* [redacted][6]; [redacted] [redacted])[7] and ([redacted][8]; and *Code of Ethics*, Sanofi Aventis (Apr. 2011).[9]

[6] [redacted]
[7] [redacted]
[8] [redacted]
[9] *See* Sanofi Code of Ethics, *available at* http://www.sanofi.us/l/us/medias/025F62A9-4642-4B95-AB1C-7CB1A2361999.pdf

38. As a result of Sanofi's actions, which were knowingly in violation of the law, Government Programs and Government Purchasers have suffered significant financial harm.

C. DEFENDANT BRISTOL-MYERS SQUIBB COMPANY

39. Defendant Bristol-Myers Squibb Company ("BMS") is a Delaware corporation with its principal corporate offices at 345 Park Avenue, New York, New York and facilities located throughout the State of New Jersey. At all times material hereto, BMS marketed and sold a range of brand pharmaceuticals and consumer medicines, including Plavix, throughout the United States, including within this judicial district. Since 1993, BMS has co-developed Plavix with Defendant Sanofi S.A. and, in November 1997, the two companies received FDA approval to market the drug in the United States under the brand name Plavix.

40. BMS markets and sells, and marketed and sold, brand-name prescription drug products, including Plavix, which are paid or reimbursed by various governmental entities and the Government Programs.

41. BMS publicly holds itself out as a company committed to high ethical standards, as well as being in compliance with fraud, waste and abuse laws enacted to prevent fraud, over-utilization, over-billing, and safeguard the health and safety of Government Program beneficiaries. *See generally U.S. Pharmaceuticals Compliance and Ethics Code of Conduct*, Bristol-Myers Squibb Company (eff. January 1, 2009).

42. BMS directed its employees to carry out the illegal scheme alleged in this Second Amended Complaint. In doing so, BMS instructed its sales force to identify themselves not as "BMS representatives," but rather as "Plavix representatives." Indeed, at various times material hereto, BMS sales representatives and Sanofi sales representatives have often conducted joint sales calls on health care providers.

43. Because of BMS' actions, which were knowingly in violation of the law, Government Programs and Government Purchasers have suffered significant financial harm.

D. DEFENDANT BRISTOL-MYERS SQUIBB SANOFI PHARMACEUTICALS HOLDING PARTNERSHIP

44. Defendant Bristol-Myers Squibb Sanofi Pharmaceuticals Holding Partnership a/k/a Bristol Myers Squibb/Sanofi-Synthelabo Partnership ("the BMS/Sanofi Partnership") is a partnership with its principal place of business at Route 206 in Province Line Road, Princeton, New Jersey 08543. The partnership, which is jointly operated by Sanofi and BMS through their facilities throughout the United States and in this judicial district, promotes the sale of Plavix. In 2006 alone, this partnership sold $3.5 billion of Plavix in the United States.

45. The BMS/Sanofi Partnership markets and sells, and marketed and sold, brand-name prescription Plavix that is paid or reimbursed by various governmental programs, including the Government Programs.

46. Sanofi and BMS knowingly contributed their employees and other resources to the perpetuation of the scheme alleged in this Second Amended Complaint through the form of the BMS/Sanofi Partnership. However, when their sales representatives have called upon health care providers to promote Plavix, they distribute business cards that identify themselves as representatives of either "Sanofi Aventis" or "Sanofi-synthelabo" or "Bristol-Myers Squibb Company," thus plainly implicating all Defendants in their misconduct.

47. Because of the BMS/Sanofi Partnership's actions, Government Programs and Government Purchasers have suffered significant financial harm.

IV. APPLICABLE LAWS

A. THE FALSE CLAIMS ACT

48. The Federal and State FCAs are, in general, *in pari material* for each other, and thus Relator frames the law using the language of the Federal FCA. Moreover, the Federal FCA will apply to nearly all claims at issue in this case, whereas each State's FCA will only apply to the subset of claims presented to Medicaid and State-provided health benefit programs (*e.g.*, to State employee health plans, State medical assistance programs, and/or State-provided medical care in prisons, hospitals and clinics) within that State and then only to the extent of that State's share of the payments made on the claims. The Federal FCA, however, does not apply to claims for payment submitted to State employee healthcare plans. As used herein, the Federal and State healthcare programs are collectively referred to as "Government Programs."

49. The Federal FCA makes it unlawful for any person to directly or indirectly deceive the Government and cause it to pay money. 31 U.S.C. § 3729 *et seq.* Relator alleges liability primarily under two of the FCA's seven liability provisions.

50. First, under the FCA's "presentment" provision, 31 U.S.C. § 3729(a)(1)(A), which imposes liability when a defendant (1) made, or caused to be made, a claim, (2) that was false or fraudulent, (3) knowing of its falsity.

51. Second, under the FCA's "false records or statements" provision, 31 U.S.C. § 3729(a)(1)(B), which imposes liability where a defendant (1) made, used, or caused to be made or used, a record or statement, (2) that was knowingly false, and (3) that was material to a false or fraudulent claim.

52. The "knowledge" element of the FCA is defined as (1) "actual knowledge of the [falsity of the] information"; (2) "deliberate ignorance of the truth or falsity of the information,"

or (3) "reckless disregard of the truth or falsity of the information" provided to the Government. 31 U.S.C. § 3729(b)(1).

53. In the present case, Relator alleges that Defendants caused healthcare providers to present claims for payment to Government Programs, where the claims were "false or fraudulent" because Defendants illegally caused healthcare providers to prescribe Plavix to patients for whom the drug was not medically reasonable and necessary due to a common genetic variant resulting in a complete lack of, or reduced production of, an enzyme necessary to activate the drug (under FDA parlance, the drug was knowingly "misbranded").

54. In addition, Defendants made, and/or caused healthcare providers to make, false records or statements material to the false or fraudulent claims, and in particular records or statements promising and/or certifying compliance with all applicable laws including those defining the limits of coverage or otherwise material to the government's decision to pay for the drug. 31 U.S.C.A. § 3729(a)(1)(B).

55. Defendants' unlawful misconduct was done "knowingly," as that term is used in the FCA. In particular, Defendants acted with at least reckless disregard for the truth of their representations concerning the safety and efficacy of Plavix, which were material to decisions by Government Purchasers and/or Government Programs to pay for Plavix.

56. Defendants' unlawful misconduct was material to the Government Programs' and Government Purchasers' decisions to pay for Plavix. Had the Government Programs and Government Purchasers known that the prescriptions were for use on patients for whom the drug was contraindicated and therefore not medically reasonable and necessary, all as the direct and intended result of Defendants' unlawful activities, it would have had a natural tendency to influence whether to make such payments.

57. It further was part of the scheme that Defendants attempted to conceal and cover up the deceptive marketing of Plavix.

B. FEDERAL HEALTH CARE PROGRAMS AND OTHER GOVERNMENT PROGRAMS

1. The Medicaid Program

58. Medicaid is a public assistance program providing for payment of medical expenses for approximately 55 million low-income patients. Funding for Medicaid is shared between the Federal Government and state governments. The Medicaid program subsidizes the purchase of more prescription drugs than any other program in the United States.

59. Medicaid is administered at the Federal level by the Secretary of the Department of Health and Human Services ("HHS"), an agency of the United States, through the Centers for Medicare and Medicaid Services ("CMS"), formerly known as the Health Care Financing Administration ("HCFA"). The Secretary promulgates rules and regulations for all participants, and monitors the states' compliance with these rules and regulations.

60. Medicaid is a state-administered program where each state sets its own guidelines regarding eligibility and services, with funding coming jointly from the states and the United States. 42 U.S.C. § 1396b.

61. The Federal portion of a state's Medicaid payments, known as the Federal Medical Assistance Percentage ("FMAP"), is based on a state's per capita income compared to the national average. *Id*. § 1396d(b). To qualify for these Federal matching funds, each state must submit a plan to the Secretary of the Department of Health and Human Services for approval. *See* 42 C.F.R. § 430 Subpart B, and § 488.303.

62. Through the FMAP process, State Medicaid administrators obtain the Federal Government's share of the ECPs' reimbursements by submitting a quarterly Form 64 to CMS. For

this reason, claims submitted to State Medicaid agencies are presented to the Federal Government within the meaning of the FCA.

63. The Federal Government also "approves" within the meaning of the FCA the claims submitted and paid through the Medicaid program. When a State presents its Form 64 (*i.e.*, the quarterly report of actual expenditures) to CMS, the amounts of any fraudulent claims the State paid will be included in those reports. Based on the information in the reports, CMS determines and approves whether the claims that the State paid with Federal funds were appropriate. If CMS determines that certain claims paid by the state were improper, CMS may recoup the amount of the erroneously expended funds by reducing the amount of money provided to the State during the next quarter.

64. Because the Form 64 constitutes the United States' means for approving and paying the amount of Federal funds expended by the State, these reports overstated the amount of Federal funds to which each State was entitled by the amount false claims Defendants caused to be submitted. They were, therefore, false records or statements that Defendants caused to be made or used to get false claims paid and approved by the United States.

65. The claims for reimbursement submitted by pharmacists to the States, which in turn caused the States to submit these claims for reimbursement to the Federal Government pursuant to FMAP, constituted false claims as a result of the claims for reimbursement for claims.

66. Although Medicaid is administered on a state-by-state basis, the state programs adhere to federal guidelines. Federal statutes and regulations restrict the drugs and drug uses that the Federal Government will pay for through its funding of state Medicaid programs.

67. Medicaid's general coverage parameters exclude items that are not "provided economically and only when, and to the extent, medically necessary," 42 U.S.C. § 1320c-5(a)(1).

In the present case, it was not medically necessary to prescribe Plavix to patients with little or none of the enzyme required to activate the drug, which resulted in exposing those patients to the drug's considerable risks with little, if any, of its benefits, as well as depriving those patients of alternative treatments.

68. In addition to the foregoing general coverage exclusions, Medicaid defines "covered outpatient drugs" coterminous with what the FDA permits in interstate commerce. 42 U.S.C. § 1396r-8(k)(2)(A)(i) (excluding coverage for drugs that are not FDA-approved under section 505 of the FD&CA [codified at 21 U.S.C. § 355]). "FDA-approved" is not a one-time event, since that status requires not only pre-market approval of the formulation and indications for use, but also the ongoing absence of various circumstances that can render a product misbranded and/or adulterated - and thereby prohibited from interstate commerce. It is hornbook law that courts will not enforce contracts for goods or services that fail to meet regulatory requirements designed to protect the public health and welfare.

69. From 2005 through 2016, Medicaid paid over $1.635 billion for Plavix, as set forth in the table below. Of this amount, at least 30%, or $490 million, was for low-responders who would not have been prescribed Plavix had Defendants provided physicians with the statutorily required "adequate information" for the safe and effective use of Plavix.

YEAR	AMOUNT
2005	$323,883,099.63
2006	$110,422,173.62
2007	$104,143,690.34
2008	$156,778,694.77
2009	$183,534,830.94
2010	$262,645,878.99
2011	$319,615,659.21
2012	$161,905,879.39
2013	$6,734,045.08
2014	$2,685,716.45
2015	$3,375,867.04

2016	$262,937.05
TOTAL:	**$1,635,988,472.51**

2. The Medicare Program

70. The Medicare Prescription Drug Improvement and Modernization Act of 2003 added prescription drug benefits to the Medicare program. Medicare serves approximately 43 million elderly and disabled Americans.

71. Like Medicaid, Medicare's general coverage parameters exclude items that are not "provided economically and only when, and to the extent, medically necessary," 42 U.S.C. § 1320c-5(a)(1). It also excludes goods and services that are not medically "reasonable and necessary for the diagnosis and treatment of illness or injury or to improve the functioning of a malformed body member." 42 U.S.C. § 1395y(a)(1)(A).

72. In addition to Medicare's general exclusions Medicare Part D adopted Medicaid's definition of "covered outpatient drugs" which is coterminous with what the FDA permits in interstate commerce. 42 U.S.C. § 1395w-102(e) and 42 C.F.R. 423.100, *incorporating by reference* 42 U.S.C. § 1396r-8(k)(2)(A)(i) (excluding coverage for drugs that are not FDA-approved under section 505 of the FD&CA [codified at 21 U.S.C. § 355]). "FDA-approved" is not a one-time event, since that status requires not only pre-market approval of the formulation and indications for use, but also the ongoing absence of various circumstances that render a product misbranded and/or adulterated - and thereby prohibited from interstate commerce. It is hornbook law that courts will not enforce contracts for goods or services that fail to meet regulatory requirements designed to protect the public health and welfare.

73. The first stage of the Medicare drug coverage program, from May 2004 through December 2005, permitted Medicare beneficiaries to enroll in a Medicare-approved drug discount card program.

74. In addition, low-income beneficiaries, defined as those whose incomes are not more than 135% of the poverty line (those with incomes of no more than $12,569 for a single person or $16,862 for a married couple in 2004) qualified for a $600 credit (funded by Medicare) on their drug discount card for 2004, and again for 2005.

75. Starting in January 2006, Part D of the Medicare Program provided subsidized drug coverage for all Medicare beneficiaries, with low-income individuals receiving the greatest subsidies. 42 U.S.C. § 1395w-101 *et seq*.

76. Part D requires beneficiaries to enroll and pay certain premiums, deductibles, co-payments, and even 100% of drug costs between a certain dollar threshold and a maximum dollar limit (the "donut hole"), that then triggers catastrophic coverage. The federal government pays 75% of actual costs between the deductible and the donut hole, and 95% of catastrophic coverage. For low-income individuals, there are various tiers in which the government pays greater percentages, up to a 100% subsidy which may be capitated.

77. Health care providers can only submit claims to Medicare if they are a registered and authorized Medicare provider. To obtain that status, a health care provider must execute a Medicare Provider Application and Provider Agreement. These documents set forth language through which the provider expressly undertakes to comply with all conditions of payment, including compliance with all relevant laws and guidance defining the limits of coverage. These documents do not obligate the health care professional to provide any goods or services to beneficiaries, and hence are part of a unilateral contract between the provider and the government.

As a unilateral contract, acceptance is evidenced by performance in the form of delivering services or goods to a beneficiary, for which the provider then submits a claim for payment to the government. In other words, the claim implicitly represents legal entitlement to payment.

78. Claims for prescription drugs also include the provider's National Provider Identifier ("NPI"), which identifies the provider as an authorized Medicare provider who has undertaken to comply with all relevant laws and guidance including those defining the limits of coverage.

79. Claims for prescription drugs also include the drug's National Drug Code ("NDC") number, which identifies the drug product by manufacturer, drug type, strength and quantity.

80. An individual is eligible to enroll in Medicare Part D if the individual lives in the service area of a Part D Plan ("PDP") and is entitled to Medicare benefits under Part A or enrolled under Part B. 42 U.S.C. § 1395w-101(a)(3)(A); 42 C.F.R. § 423.30(a). Part D benefits are provided by a PDP sponsor, which is either a prescription drug plan, a Medicare Advantage organization that offers a Medicare Advantage prescription drug plan (MA-PD plan), a PACE organization offering a PACE plan including qualified prescription drug coverage, or a cost plan offering qualified prescription drug coverage. 42 C.F.R. § 423.4.

81. The PDP sponsor is required to provide qualified prescription drug coverage, which includes "standard prescription drug coverage" or "alternative prescription drug coverage" with at least actuarially equivalent benefits. 42 U.S.C. § 1395w-102; 42 C.F.R. § 423.104(c). The program offers consumers various options which are not relevant here.

82. Medicare Part D pricing is based on a quasi-free market model. At the end of the day, however, it is still a per-item payment system. Below, Relators provide the basic contours of the Medicare Part D system.

83. Medicare contracts with private Part D providers (also known as "sponsors" or "contractors") to administer prescription drug plans.

84. A sponsor must submit a bid in the year prior to the calendar year in which Part D benefits will be delivered. *See* 42 C.F.R § 423.265. The bid contains a per member per month (PMPM) cost estimate for providing Part D benefits to an average Medicare beneficiary in a particular geographic area. From these bids, CMS calculates nationwide and regional benchmarks which represent the average PMPM cost. If the Part D sponsor's bid exceeds the benchmark, the enrolled beneficiary must pay the difference as part of the monthly beneficiary premium.

85. CMS provides each sponsor with a direct subsidy in the form of advance monthly payments equal to the Part D plan's standardized bid, risk adjusted for health status, minus the monthly beneficiary premium, estimated reinsurance subsidies for catastrophic coverage, and estimated low-income subsidies. 42 C.F.R. §§ 423.315, 423.329.

86. In the year following the benefit year, there is a reconciliation based on the actual claims paid for the Part D sponsor's member beneficiaries, and an adjustment is made so that Medicare Part D is ultimately only paying for the drugs actually dispensed.

87. Of key importance here, sponsors must certify in their contracts with CMS their agreement to comply with all federal laws and regulations designed to prevent fraud, waste, and abuse. 42 C.F.R. § 423.505(h)(1). In turn, the sponsor's contracts with downstream entities, including pharmacies and Pharmacy Benefit Managers ("PBMs"), must contain similar language obligating those entities to comply with all applicable federal laws, regulations, and CMS instructions when submitting Part D claims data or otherwise acting as the sponsor's agent. 42 C.F.R. § 423.505(i)(4)(iv).

88. When a pharmacy dispenses drugs to a Medicare beneficiary, it submits a claim electronically to the beneficiary's Part D plan (usually via the sponsor's contracted PBM) and receives reimbursement from the plan sponsor for the portion of the drug cost not paid by the beneficiary.

89. The sponsor (again usually through its contracted PBM) then notifies CMS that a drug has been purchased and dispensed by means of a document called a Prescription Drug Event record ("PDE"), which is an electronically created document that includes 37 fields of information including the amount paid to the pharmacy. Submission to CMS of truthful and accurate PDEs for each prescription is a condition of payment.

90. In the year following the benefit year, CMS uses a sponsor's PDEs to compare the sponsor's actual prescription drug costs to CMS's advance payments to the sponsor. If a sponsor's actual costs exceed the sums it received from CMS for the year, the plan sponsor recoups its losses from CMS. Conversely, if a sponsor's actual costs were less than the sums it received from CMS for the year, CMS recoups the overpayments by reducing subsequent payments to the sponsor. These reconciliation payments are subject to application of certain statutorily defined risk-sharing corridors.

91. Sponsors subcontract with many entities to provide drugs to the Medicare Part D beneficiaries enrolled in their plans. These include subcontracts with PBMs that provide drugs through mail order operations and pharmacy chains which provide drugs on a retail level.

92. The table above, at ¶ 69, reflects that Medicaid reimbursements for Plavix dropped by $213 million in 2006, which was due to the fact that starting in 2006 Medicare Part D began to pay for outpatient drugs when persons are eligible under both programs. Using a baseline of $213 million for 2006, and assuming modest growth in-line with the

double-digit Medicaid reimbursement growth, Relator estimates that from 2006 through 2016 Medicare paid at least $1.5 billion for Plavix, of which at least 30%, or some $450 million, was for low-responders who would not have been prescribed Plavix had Defendants provided physicians with the statutorily required "adequate instructions" to use the drug safely and effectively.

93. In its SEC Form 20F for fiscal year 2006, Sanofi also noted that "the new Medicare Part D drug benefit program, combined with Medicaid and other federal programs, establishes the federal government as almost equal to the private health insurance sector in terms of total drug reimbursement." Plavix sales in the U.S. are summarized below (note the dramatic drop in 2012 reflects the emergence of generic equivalents in May 2012)

YEAR	AMOUNT (billions)
2000	$0.9
2001	$1.1
2002	$1.9
2003	$2.5
2004	$3.3
2005	$3.8
2006	$3.2
2007	$4.8
2008	$5.5
2009	$6.6
2010	$6.2
2011	$6.6
2012	$1.5
TOTAL:	**$46.9**

94. Based on the foregoing, U.S. taxpayers have paid over $20 billion for Plavix, of which at least 30%, or $6 billion, was prescribed to low-responders who received nothing more than a placebo.

3. Reimbursement Under Other Federal Health Care Programs

95. In addition to Medicaid and Medicare, the Federal Government reimburses a portion of the cost of prescription drugs under several other federal health care programs. For example:

(i) CHAMPUS/TRICARE is a health care program administered by the Department of Defense for individuals and dependents affiliated with the armed forces.

(ii) CHAMPVA is a health care program administered by the Department of Veterans Affairs for families of veterans with 100% service-connected disabilities.

(iii) The FEHBP provides health insurance for federal employees, retirees and survivors, and it is administered by the Office of Personnel Management.

(iv) Each State offers health benefits to its employees and certain of its citizens through various programs administered by the States, which include prescription drug benefits.

(v) Each State offers various health benefits in its corrective institutions, state hospitals, and through various child health programs, including prescription drug benefits.

96. From 2005 through 2016, these programs paid hundreds of millions of dollars for Plavix, of which over 30% was for low-responders who would not have been prescribed Plavix had Defendants provided physicians with the statutorily required "adequate instructions" to use the drug safely and effectively.

C. THE FOOD AND DRUG ADMINISTRATION ("FDA") REGULATORY SYSTEM

1. The FDA Regulates What Drugs May Be Marketed, and the Uses for which They May Be Marketed.

97. Under the Food, Drug and Cosmetics Act ("FDCA"), 21 U.S.C. §§ 301-97, new pharmaceutical drugs cannot be marketed in the United States unless the sponsor of the drug demonstrates to the satisfaction of the FDA that the drug is safe and effective for each of its

intended uses in the general adult population. 21 U.S.C. § 355(a), (d). Approval of the drug by the FDA is the final step in a multi-year process of study and testing.

98. To determine whether a drug is "safe and effective," the FDA relies on information provided by a drug's manufacturer; it does not conduct any substantial analysis or studies itself. Applications for FDA approval (known as New Drug Applications or "NDAs") must include "full reports of investigations which have been made to show whether or not such drug is safe for use and whether or not such drug is effective in use." 21 U.S.C. § 355(b)(1)(A).

99. Under the nation's food and drug laws, a drug may not be introduced into interstate commerce unless its sponsor has shown that the drug is safe and effective for the intended conditions of use. *See* 21 U.S.C. § 321. The law requires that "adequate and well-controlled investigations" be used to demonstrate a drug's safety and effectiveness. *See* 21 U.S.C. § 355(d)(7). The FDA approves a drug if there are "adequate and well-controlled clinical trials" that demonstrate a drug's safety and effectiveness for its "intended conditions" of use. *See* 21 U.S.C. § 355(d)(5). The "intended conditions" for use of a drug are listed in the drug's labeling, which is reviewed and approved by the FDA. *See* 21 U.S.C. § 355(d)(1)-(2). Indications for use that are not listed in a drug's labeling have not been approved by the FDA. *See* 37 Fed. Reg. 16,503 (1972).

100. Important here, the manufacturer has a duty to ensure that the drug's labeling provides physicians with "adequate instructions" to use the drug safely and effectively. *See* 21 U.S.C. § 352(a) and (f)(1), and 21 C.F.R. § 201.100.

101. After a drug is approved, the FDA continues to exercise control over the product labeling. To protect patients from safety concerns, the FDA may: require a labeling change to reflect newly determined contra-indications for use, the increased risk of various side effects or

interactions, or to restrict a drug's indications; or, in extreme cases, force a withdrawal from the market. *See* 21 C.F.R. § 201.57(3).

102. The manufacturer, however, is not required to wait for the FDA to approve changes to the label. Federal regulation permits a drug manufacturer to change the label to "add or strengthen a contraindication, warning, precaution, or adverse reaction" or to "add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product," and seek FDA approval after the fact. 21 C.F.R. § 314.70(c)(6)(iii)(A), (C). Although a 2008 amendment indicated that such label changes may only be made "to reflect newly acquired information," 73 Fed. Reg. 49609, the FDA clarified that "newly acquired information" includes "new analyses of previously submitted data," *id*. at 49604.

103. Relevant here, a drug's label must include a section entitled "Contraindications" providing "[a] concise statement of each of the product's contraindications, as required under paragraph (c)(5) of this section, with any appropriate subheadings." 21 C.F.R. § 201.57(a)(9). Paragraph (c)(5), in turn, states:

> (5) Contraindications. This section must describe any situations in which the drug should not be used because the risk of use (e.g., certain potentially fatal adverse reactions) clearly outweighs any possible therapeutic benefit. Those situations include use of the drug in patients who, because of their particular age, sex, concomitant therapy, disease state, or other condition, have a substantial risk of being harmed by the drug and for whom no potential benefit makes the risk acceptable. Known hazards and not theoretical possibilities must be listed (e.g., if severe hypersensitivity to the drug has not been demonstrated, it should not be listed as a contraindication). If no contraindications are known, this section must state "None."

Id. § 201.57(c)(5).

2. The FDA Requires Drug Companies to Disclose Information Regarding Approved Drugs' Safety and Effectiveness and as Well as Reports of Adverse Events

104. Pursuant to Section 505 of the FDCA, 21 U.S.C. § 355, and 21 C.F.R. § 314.81, Defendants, as the original applicants for approval to market Plavix in the United States, have been required to submit annual reports to the FDA that include, among other things: (i) "[a] brief summary of significant new information from the previous year that might affect the safety, effectiveness, or labeling" of Plavix; (ii) "[r]eports of experiences, investigations, studies, or tests involving chemical or physical properties, or any other properties" of Plavix; and (iii) "published clinical trials of [Plavix] (or abstracts of them), including clinical trials on safety and effectiveness; clinical trials on new uses; biopharmaceutic, pharmacokinetic, and clinical pharmacology studies; and reports of clinical experience pertinent to safety . . . conducted by or otherwise obtained by [Sanofi and BMS, as the applicant]." 21 C.F.R. 314.81(b)(2). The purpose of this requirement is to enable the FDA to determine whether there is or may be grounds to withdraw or modify its approval of a new drug application.

105. Further, drug companies like Defendants are required by law to report adverse events, including "any failure of expected pharmacologic action." 21 C.F.R. § 314.80 (governing post-marketing reporting of adverse drug experiences). Although the original version of this regulation required a report of "any *significant* failure of expected pharmacologic action" (emphasis added), the FDA amended the regulation in 1989 to delete the word "significant" because it "consider[ed] any report of failure of a drug to produce the expected pharmacological action to be significant." 54 Fed. Reg. 28,872 at 28,889 (July 10, 1989). The FDA also concluded that by deleting the word "significant" from the regulation, it thereafter "would unambiguously require that *all reports of a therapeutic failure (lack of effect)* be submitted to FDA." *Id*. (emphasis added). The public policy objective behind the change was clear: "[A] complete picture of adverse drug experiences, rather than selected reports, [would] improve the [FDA's] ability to determine

whether it should take regulatory action." 57 Fed. Reg. 17,950 at 17,983 (Apr. 28, 1992. As applied to this case, a loss or failure of efficacy in a significant portion of the population represents a complete failure of the "expected pharmacologic action" that Defendants were required to report to the FDA.

3. FDA Regulations Prohibit False and Misleading Statements about a Drug's Use.

106. FDA regulations restrict how drug companies may market and promote approved drugs. *See* 21 U.S.C. §§ 331, 352; 21 C.F.R. § 314.81. Drug labels—including all marketing and promotional materials relating to the drug—may not describe intended uses for the drug that have not been approved by the FDA. 21 U.S.C. §§ 331, 352. Illegal "misbranding" can result in criminal penalties. *See id*. § 333.

107. The same general requirements about the promotion of prescription drugs apply to both professional and consumer-oriented marketing. In particular, promotional materials may only make claims that are supported by "substantial" scientific evidence (according to strict scientific procedures) and they may not be false or misleading. FDA oversight helps ensure a "fair balance" in all promotional claims and materials. Federal regulations require that the risks, as well as the benefits, be clearly identified and given appropriate prominence. Promotional materials must be consistent with the FDA-approved product labeling. This restriction pertains to the clinical indications for which the drug has been approved as well as the dosing regimen that is supported by the clinical trials that were undertaken to establish safety and efficacy.

108. The law prohibits drug manufacturers from marketing or promoting a drug for a use that the FDA has not approved, or for a patient group that is unapproved. Specifically, a manufacturer illegally "misbrands" a drug if the drug's labeling (which includes all marketing and promotional materials relating to the drug) describes intended uses for the drug that have not been

approved by the FDA. 21 U.S.C. §§ 331, 352; *see also* Final Guidance on Industry-Supported Scientific and Educational Activities, 62 Fed. Reg. 64,074 (Dec. 3, 1997). The FDA "interprets the term 'advertisement' to include information (other than labeling) that originates from the same source as the product and that is intended to supplement or explain the product."

109. Any manufacturer speech explaining one of its products is an "advertisement" for the product and is subject to the FDA's "fair balance" requirement, described below.

110. Title 21 of the Code of Federal Regulations provides that an advertisement may not use "literature, quotations, or references for the purpose of recommending or suggesting conditions of drug use that are not approved or permitted in the drug package labeling." 21 C.F.R. § 202.1(e)(6)(xi); *see also* 21 U.S.C. § 331(d) (prohibiting distribution of a drug for non-approved uses); *id*. § 331(a) (prohibiting distribution of a misbranded drug).

111. The regulations require drug companies to present a "true statement" of information relating to the side effects, contraindications and effectiveness of the drug use. *See* 21 C.F.R. § 202.1(e)(5). A company violates this regulation if it presents "false or misleading" information about a drug's side effects or does not "fair[ly] balance" information relating to the safety and efficacy of the drug use against information about its side effects and contraindications. *Id*.

112. These regulations lay out the stringent requirements that must be met by the manufacturer before it may disseminate any materials on uses of marketed drugs. 21 C.F.R. § 99.101 *et seq*. This material must be in the form of an unabridged reprint or copy of a published, peer-reviewed article that is considered "scientifically sound" by experts qualified to evaluate the safety or effectiveness of the drug involved. *See id*. § 99.101(a)(2).

113. Furthermore, the manufacturer must not disseminate materials that are "false and misleading," such as those that only present favorable information when unfavorable publications

exist, exclude mandatory information about the safety and efficacy of the drug use, or present conclusions that "clearly cannot be supported by the results of the study." *Id*. § 99.101(a)(4).

114. In sum, the FDA regulatory regime protects patients and consumers by ensuring that drug companies do not promote drugs for uses, and upon populations, other than those found to be safe and effective by an independent, scientific government body—the FDA. And the prohibition on unsubstantiated claims protects patients and consumers by ensuring that the prescription and use of approved drugs is not based on misleading marketing tactics.

115. The FDCA specifically prohibits from introduction or delivery for introduction into interstate commerce, and the interstate transportation of drugs that are misbranded or otherwise in violation of 21 U.S.C. § 355. 21 U.S.C. § 331(a), (c), (d), (k); *see* 21 U.S.C. § 352; 21 U.S.C. § 355(a), (d) and (e). The FDCA also prohibits misbranding a drug while it is in interstate commerce, or while held for sale after shipment in interstate commerce, and prohibits the alteration of a drug's labeling. 21 U.S.C. § 331(b) and (k). Thus, these prohibitions reach the activities of "wholesalers, retailers, pharmacies, and hospitals, as well as manufacturers." *See* 55 FR 38020 at Comment 25 (specifically referencing scope of subsection (k) concerning drugs held for sale).

116. These sections make clear that, even though a drug may have received "FDA-approval" of its formulation, indications for use, and dosage, the actual drug product is not in its FDA-approved form if it is subsequently either misbranded or adulterated.

117. The FDCA's definition of misbranding covers various issues. Those at issue in this action include: "(a) [i]f its labeling is false or misleading in any particular; [and] (f) [failure to provide] adequate directions for use." 21 U.S.C. § 352(a) and (f)(1), and 21 C.F.R. § 201.100.

118. The FDCA defines "misbranded" to include any "labeling" that is false or misleading in any respect as to various factors, including safety and efficacy. 21 U.S.C. § 352(a).

119. Hence, to the extent *any communication* is made by or on behalf of a manufacturer that is materially false or misleading concerning the efficacy of a drug, including any failure to fairly and accurately represent required information, then the drug is misbranded and prohibited from interstate commerce.

120. In this case, since as early as 1998 Defendants have made false and misleading statements all across the United States about the efficacy of Plavix for all antithrombotic and antiplatelet population groups, and the appropriateness of using a loading dose greater than 300mg.

121. A drug whose labeling fails to provide adequate "directions for use" to laypersons, or adequate "instructions for use" to prescribing medical professionals, constitutes a separate and independent basis for being misbranded and barred from interstate commerce, and therefore ineligible for payment by the government.

V. DEFENDANTS' FRAUD

122. Atherosclerosis is a systemic disease effecting arteries throughout the body. It results from a life-long tendency to accumulate plaque in the arterial wall which, as it progresses, can lead to heart attacks and strokes. Platelets play an important role in the development of chronic atherosclerosis and in the acute pathophysiology of plaque rupture which causes heart attacks and strokes. Anti-platelet therapy is the most important component of the treatment for atherosclerosis, since it is given to prevent the lethal/disabling event.

123. The treatment of atherosclerotic coronary artery disease falls into three broad categories. In order of lowest to highest cost and risk, they are: (i) medical therapy; (ii) revascularization by percutaneous coronary intervention ("PCI"), which in the majority of cases involves stent placement; and (iii) surgical revascularization via coronary artery bypass surgery ("CABG"). Knowing whether a patient is responsive or non-responsive to Plavix would have had a significant impact upon the clinical decision making process throughout the years that Plavix has

been available to clinicians, since placing a stent in the coronary artery is associated with the marked enhancement of the risk of developing a thrombus. Plavix is given to prevent that event and to make stenting a safe alternative to CABG (coronary bypass surgery).

124. One of the leading medical therapies for this condition is the use of antiplatelet drugs. Because they promote arterial circulation and decrease the ability of blood clots to form, such drugs have been widely used in primary and secondary prevention of thrombotic cerebrovascular or cardiovascular disease. Antiplatelet agents are the most important agents administered to patients at high risk for arterial clot formation—*i.e.*, those with a history of heart attack, coronary stenting or stroke.

125. The dominant drug in this class is Plavix (clopidogrel), an oral tablet formulation of clopidogrel bisulfate. Plavix was first approved by the FDA on November 17, 1997 for the reduction of atherosclerotic events (myocardial infarction, stroke and vascular death) in patients with atherosclerosis documented by recent stroke, recent myocardial infarction or established peripheral arterial disease ("PAD"). Several years later, on February 27, 2002, the FDA approved Plavix for the treatment of patients with Acute Coronary Syndrome (unstable angina/non-ST-elevation myocardial infarction)—also known as "NSTEMI." And on August 17, 2006, the FDA approved Plavix for the treatment of patients with Acute Coronary Syndrome (ST-elevation myocardial infarction)—also known as "STEMI."

126. From March 1998 until May 17, 2012 Plavix was marketed in the United States by Defendants through the BMS/Sanofi Partnership. Until its patent expiration in 2012, Plavix was among the top selling drugs in the U.S. with sales of $3.8 billion in 2005, $3.2 billion in 2006, $4.8 billion in 2007, $5.5 billion in 2008, $6.6 billion in 2009, $6.15 billion in 2010, $6.56 billion in 2011, $1.5 billion in 2012, and $258 million in 2013.

127. Since it was first introduced in 1998, Plavix has played a critical role in treating patients suffering life threatening conditions associated with myocardial infarction with ST-elevation, non-ST elevation myocardial infarction or unstable angina, or those suffering ischemic heart disease. In fact, Plavix is the most important drug administered to the high-risk patient to prevent the vascular catastrophe—*i.e.*, the clot, which usually results in sudden death.

128. If prescribers, purchasers and payors had known Plavix lacked demonstrable pharmacodynamic effect in over 30% of patients—and that there were means available to identify these patients—it is likely that they would have made different treatment decisions for these patients.

129. Knowing whether a patient is responsive or non-responsive to Plavix would have had a significant impact upon the clinical decision making process throughout the years that Plavix has been available to clinicians. Placing a stent in the coronary artery is associated with a higher risk of developing a thrombus. Plavix is given to prevent that event and to make stenting a safe alternative to CABG (coronary bypass surgery).

130. For example, once a patient is given Plavix, the increased risk of bleeding precludes CABG surgery as an option until the drug has been sufficiently expelled by the body, which takes several days. Knowing this, one of Defendants' insidious strategies was to promote Plavix as the unquestioned protocol for *all* ACS patients treated by first responders in ambulances and emergency rooms, notwithstanding Defendants' knowledge that it was ineffective for over 30% of patients.

A. DR. GURBEL UNCOVERS THE VOR ISSUE

131. Since at least [redacted], Defendants have known that over 30% of patients had little or no response to Plavix. This issue was brought to Defendants attention by [redacted]

[redacted]. As noted in a [redacted][10] the [redacted] had revealed that [redacted].[11] In short, for over 30% of patients the drug was contraindicated and therefore essentially a medically unnecessary and unreasonable placebo. Rather than publish this information, Defendants concealed it from physicians and regulators in the United States.

132. Although Defendants' [redacted] did not reveal why over 30% of patients were low-responders, based on their [redacted] Defendants plainly should have fulfilled their legal obligation to update the United States' Plavix labeling to reflect this adverse efficacy data and ensure that physicians were provided with "adequate instructions" to use Plavix safely and effectively.

133. Since shortly after Plavix was first introduced to the market, Dr. Gurbel's research has paved the way in understanding the effects and development of antiplatelet agents. His laboratory pioneered the concept of antiplatelet response variability, and his research and observations led to the development of new $P2Y_{12}$ inhibitors.[12]

134. Dr. Gurbel communicated regularly with Defendants about clopidogrel resistance in the late 1990s and early 2000s. In fact, he received a grant from Defendants in the late 1990s to conduct the first prospective study of the antiplatelet effects of Plavix in patients undergoing stenting, where he and his colleagues first saw the lack of response (defined as <10% inhibition of platelet aggregation) in over 30% of the patients studied. This was the PRONTO study, as to

[10] [redacted].
[11]
[12] $P2Y_{12}$ is a protein found mainly but not exclusively on the surface of blood platelets, and is an important regulator in blood clotting.

which, when Defendants reviewed a draft of the abstract in July 2000, they were certain that "[redacted].[13] Despite the extraordinary significance of these findings, the study was not published in major cardiovascular journals where it would have been widely seen and regarded by cardiologists—and spurred funding for further analysis—but instead was buried in the relatively unknown AMERICAN HEART JOURNAL.

135. This lack of a uniform antiplatelet response, also called "Variability of Response" ("VOR") or "Variability of Platelet Reactivity" ("VPR") (hereinafter "VOR"), occurred in around 30% of patients. These patients were regarded as "non-responders" or "low responders." Based on an absence or near absence of a measurable pharmacodynamic effect, it was immediately obvious to Gurbel that these patients were not receiving the primary or secondary prevention effect needed to prevent thrombosis, the formation of a blood clot inside a blood vessel (frequently around a stent[14]), obstructing the flow of blood through the circulatory system.

136. Based on his preliminary research, Dr. Gurbel subsequently communicated with Chitra Sekaran (SA), and other individuals, seeking Defendants' support for studies investigating various dimensions of clopidogrel resistance primarily in the treatment of patients undergoing stenting. Gurbel was also very concerned about the lack of effect of this drug in patients treated with Plavix for other reasons—such as patients with peripheral vascular disease and stroke. Multiple times, at various meetings, he proposed imbedding platelet function testing in several of Defendants' future studies so that variability of response could be studied. Gurbel's efforts, however, were met with interminable delays, purportedly because Defendants were prioritizing

[13] [redacted]

[14] A stent is a metal or plastic tube inserted into the lumen of an anatomic vessel or duct to keep the passageway open.

other studies, such as CHARISMA and ACTIVE.[15] Dr. Gurbel eventually learned that Defendants had an internal mandate that they would not approve studies which included platelet aggregation testing as part of the protocol, which automatically excluded his research proposals.

137. As Defendants [redacted], Dr. Gurbel was the primary investigator and author of studies creating the public knowledge that clopidogrel had a significant variability of response, which in turn compelled Defendants to [redacted].

138. In particular, on March 19, 2001 at the American College of Cardiology meeting in Orlando, Florida and again on September 4 , 2001 at the XXIII Congress of the European Society of Cardiology in Stockholm, Sweden, Dr. Gurbel first reported that the percentage of patients meeting the empirical definition of resistance to clopidogrel ("an absolute difference between baseline aggregation and posttreatment aggregation of 10% or less with 5 µmol/L ADP used as the agonist") was 63% two-hours after administration, 31% both 24-hours and 5-days after administration, and 15% 30-days after administration. *See* Paul A. Gurbel, *et al*., *Clopidogrel for Coronary Stenting: Response Variability, Drug Resistance, and the Effect of Pretreatment Platelet Reactivity*, 107 CIRCULATION 2908-13, at 2909-10 (2003) (concluding that "[i]nterindividual variability in the platelet inhibitory response from [Plavix] occurs in patients undergoing elective coronary stenting").

139. In response, [redacted] Defendants [redacted].[16]

15 [redacted]

16 [redacted]

140. Early on, Defendants understood Dr. Gurbel's research as a threat to Plavix. [redacted] „[17]

141. [redacted] [18] [redacted] [19]) [redacted] [20] This study, however, would not be published until 2009. *See* Bal Dit Sollier, Claire, *et al., Functional variability of platelet response to clopidogrel correlates with P2Y 12 receptor occupancy,* 101 THROMB. HAEMOST. 116-22 (2009).

142. During this entire time, from [redacted] through 2009, as Defendants' own knowledge that over 30% of patients were low responders was increasingly bolstered by Dr. Gurbel's published scientific studies, Defendants never fulfilled their legal obligation to update the United

17 [redacted]
18 [redacted]
19 [redacted]
20 [redacted]

States' Plavix labeling to reflect this adverse efficacy data and ensure that physicians were provided with "adequate instructions" to use Plavix safely and effectively.

143. Ultimately, in 2009, Dr. Gurbel as senior author along with principal investigator Alan R. Shuldiner, MD and others co-authored a study that conclusively identified a common variant of the CYP2C19 gene as a major factor for clopidogrel non-responders and low-responders. Alan R. Shuldiner, MD, *et al.*, *Association of Cytochrome P450 2C19 Genotype with the Antiplatelet Effect and Clinical Efficacy of Clopidogrel Therapy*, 302 JAMA 849-58 (August 26, 2009). Once again, Defendants [redacted][21] Gurbel's results conclusively showed that Plavix resistance was associated with genetic mutation was a huge observation, and were in stark contrast to a prior paper endorsed by Defendants implying that Plavix variability of response was nothing more than the "normal" variability expected with all drugs. V. Serebruany, *et al.*, *Variability in Platelet Responsiveness to Clopidogrel Among 544 Individuals*, 42 J. AM. COLL. CARDIOL. 246-51 (2005) (hereafter, the "Serebruany Study"). In other words, Plavix response variability went from an expected normal response (as advocated by Defendants) to an abnormal event linked to a genetic mutation.

144. Based on the evidence that Dr. Gurbel and his colleagues (along with the work of others) had assembled of genetically determined low-responders and non-responders with significance for clinical outcomes, the FDA stepped in and required Defendants to include a Black Box Warning in the Plavix labeling starting in March 2010.

[21] [redacted] (Press Releases).

B. INDEPENDENT STUDIES EMERGE SUBSTANTIATING DR. GURBEL'S VOR FINDINGS

145. Notwithstanding Defendants' efforts to [redacted][22]), studies began to emerge that increasingly corroborated Dr. Gurbel's findings: first, in 2002-2005, by quantifying the diminished response affected up to 40% of patients; then, in 2006, confirming that CYP2C19 polymorphisms result in diminished response; and finally, in 2009, quantifying that CYP2C19 polymorphisms resulted in diminished response in up to 35% of patients.

146. In 2002 and 2003, several published studies established a distinction among responders and non-responders to Plavix therapy. Individual variations in platelet inhibition after treatment with clopidogrel were first reported by other researchers in 2002. *See* P. Järemo, *et al*., *Individual variations of platelet inhibition after loading doses of clopidogrel*, 252 J. INTERNAL MED. 233-38 (2002) (concluding that Plavix "evoked platelet inhibition exhibits a considerable individual heterogeneity"). *See also* I. Müller, *et al.*, *Prevalence of clopidogrel non-responders among patients with stable angina pectoris scheduled for elective coronary stent placement*, 89 J. THROMB. HAEMOST. 783-87 (2003) (concluding that "a subgroup of patients undergoing [percutaneous coronary intervention] does not adequately respond to [Plavix], which may correspond to the occurrence of thromboischemic complications"); D. Soffer, *et al*., *Impact of Angina Class on Inhibition of Platelet Aggregation Following Clopidogrel Loading in Patients Undergoing Coronary Intervention*, 59 CATH. & CARDIO. INTERV. 21-25 (2003) (finding "significant interpatient variability in the degree of platelet inhibition" and suggesting "resistance to clopidogrel").

[22] [redacted]

147. Several articles published in 2004 and 2005 further confirmed what Dr. Gurbel had first reported in 2001. *See* J.E. Mobley, *et al*., *Frequency of Nonresponse Antiplatelet Activity of Clopidogrel During Pretreatment for Cardiac Catheterization*, 93 AM. J. CARDIO. 456-58 (2004) ("Recent investigations have indicated that 20% to 30% of patients fail to attain platelet inhibition after clopidogrel therapy."); D.J. Angiolillo, *et al*., *Identification of low responders to a 300-mg clopidogrel loading dose in patients undergoing coronary stenting*, 115 THROMB. RES. 101-08 (2005) ("Identification of clopidogrel low responders before intervention appears to be an emerging critical direction for tailoring antiplatelet therapy to ensure a more effective antithrombotic protection in these patients.").

148. Although these studies did not specifically address the CYP system or the CYP2C19 enzyme in particular, Defendants should nevertheless have complied with their legal obligation to ensure that the Plavix labeling (including the package insert and all product communications) provided physicians with "adequate instructions" to use the drug safely and effectively. Updating the labeling in this manner would have also required that Defendants notify the FDA that: (i) there was a growing body of evidence that a substantial portion of the patient population would have diminished or no responsiveness to Plavix; and (ii) adverse clinical implications of such responsiveness had been reported. They did not do so.

149. Defendants failed to bring this information directly to the attention of physicians to whom they were actively promoting Plavix for the treatment of all antithrombotic and antiplatelet conditions, all the while telling doctors that they were providing them with all the pertinent efficacy and safety information regarding the drug. Instead, Defendants sponsored and helped write studies attempting to downplay the scope and significance of the VOR issue.

150. For example, in 2005, the JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY published the results of Serebruany Study—*that received research support and drafting guidance from Defendants themselves*—into the responsiveness of 544 individuals to Plavix therapy. The authors noted that their work had been prompted by "a number of reports" that "dichotomized patients who are treated with [Plavix] into a minority of 'non-responders' and a majority of 'responders.'" The authors concluded that "there is a very large range of responsiveness to ex vivo testing" in patients treated with Plavix which, if it corresponds to clinical outcomes, means "it is likely that a small but significant portion of patients are receiving inadequate protection from thrombotic events despite currently standard antiplatelet therapy, whereas a similar proportion may be at higher risk for bleeding complications." *See* V. Serebruany, *et al.*, *Variability in Platelet Responsiveness to Clopidogrel Among 544 Individuals*, 42 J. AM. COLL. CARDIOL. 246-51 (2005).

151. Plainly, the reports that prompted the Serebruany Study, as well as the conclusions of the Serebruany Study itself, pointed to significant adverse efficacy data—despite Defendants' efforts to control the drafting and soften the data's implications. Having sponsored the Serebruany Study, Defendants clearly were aware of its conclusions, and they should have updated the Plavix labeling to ensure physicians had "adequate instructions" to use Plavix safely and effectively, and pursued and reported those conclusions to the FDA and the physicians to whom they were promoting the drug. *See* 21 C.F.R. § 314.81(b)(2). However, there is no indication that Defendants did any of those things. Instead, as alleged below, Defendants continued to work aggressively to deflect VOR claims so they could continue to grow the market for Plavix by employing an "Expand & Protect" strategy which would put increasing numbers of patients at risk.

152. Not long after the Serebruany Study was published, the Journal of the American College of Cardiology published (in February 2006) an abstract that concluded:

> These results indicate that subjects with a CYP2C19*2 allele generate less active metabolite of [Plavix] and this is associated with a diminished pharmacodynamic response. Variation in CYP-mediated metabolism may be a significant contributing factor to the previously reported inter-patient variability in the pharmacodynamic response to [Plavix].

See J. Brandt, *et al.*, *CYP2C19*2 Polymorphism Contributes to a Diminished Pharmacodynamic Response to Clopidogrel* [abstract], 47 J. AM. COLL. CARDIOL. 380A (2006) (the "Brandt Study"). With these conclusions to bolster those of Dr. Gurbel and others, there could be no question after February 2006 that there was significant adverse efficacy data traceable to a specific pharmacokinetic mechanism. Defendants should have reported this to the FDA and treating physicians in order to comply with their legal duty to update the labeling and ensure physicians had "adequate instructions" to use Plavix safely and effectively. However, there is no indication that they even contemplated doing so.

153. Shortly after the Brandt Study was published, the American Society of Hematology published a study in June 2006 whose authors corroborated Dr. Gurbel's findings, observing that "pharmacodynamic response to [Plavix] varies widely from subject to subject, and about 25% of patients treated with standard [Plavix] doses display low ex vivo inhibition of ADP-induced platelet aggregation," and concluded that "response to [Plavix] was strongly influenced by the CYP2C19 genotypic status." *See* J-S. Hulot, *et al.*, *Cytochrome P450 2C19 loss-of-function polymorphism is a major determinant of clopidogrel responsiveness in healthy subjects,* 108 BLOOD 2244-47 (2006); *cf.* J.T. Brandt, *et al.*, *Common polymorphisms of CYP2C19 and CYP2C9 affect the pharmacokinetic and pharmacodynamic response to clopidogrel but not prasugrel*, 5 J. THROMB. HAEMOST. 2429-36 (2007) ("common loss of function polymorphisms of CYP2C19 and CYP2C9 are associated with decreased exposure to the active metabolite of clopidogrel" which is "associated with a diminished pharmacodynamic response"); S.M.G. Smith, *et al.*, *Common sequence variations in the $P2Y_{12}$ and CYP3A5 genes do not explain the variability in the inhibitory*

effects of clopidogrel therapy, 17 PLATELETS 250-58 (June 2006) ("antiplatelet effects of clopidogrel . . . demonstrate wide inter-individual variability and patients with clopidogrel resistance may be at increased atherothrombotic risk"); *see also* P.A. Gurbel, *et al*., *Drug Insight: clopidogrel nonresponsiveness*, 3 NAT. CLIN. PRAC.: CARDIO. 387-95 (2006) ("Clopidogrel nonresponsiveness is a consistent phenomenon observed in multiple research studies.").

154. With evidence from Dr. Gurbel and others now identifying the genetic cause of low-response to Plavix, Defendants plainly should have timely updated the Plavix labeling to reflect this adverse efficacy data and ensure that physicians were provided with "adequate instructions for use." Defendants also plainly should have reported this adverse efficacy data to the FDA and to the tens of thousands of treating physicians to whom they were promoting Plavix as appropriate for all antithrombotic and antiplatelet patients. Defendants, however, refused to do so, instead developing a strategy to protect Plavix market share at all costs: "[redacted][23]

155. By 2005, it was clear to Dr. Gurbel and other leading researchers that (i) Plavix must be transformed into an active metabolite by CYP enzymes in order for it to have the desired antiplatelet effect; (ii) the CYP2C19 enzyme plays an important role in metabolizing Plavix; (iii) the genes encoding the CYP enzymes are polymorphic, meaning that they contain multiple alleles (*i.e.*, one of two or more alternative forms of a gene that arise by mutation and are found at the same place on a chromosome); and (iv) common alleles of the CYP enzyme gene lead to reduced functionality, and thus diminished or no responsiveness to Plavix. However, there is no indication that Defendants brought this information to the attention of the FDA, as was required

[23] [redacted]

by the FDCA and applicable regulations, or physicians to whom they were promoting the drug. In fact, Defendants (as alleged herein) did just the opposite.

156. Defendants' efforts had successfully contained the VOR research like Dr. Gurbel's to a few small trials, which had received relatively limited attention. Even so, Defendants were acutely aware of the few VOR studies Dr. Gurbel and others had succeeded in getting published, [redacted]. For example, [redacted]. Even while Dr. Gurbel and others had succeeded in publishing a few VOR research papers, Defendants [redacted].[24] While Defendants had successfully limited VOR publications, they noted this may [redacted].[25]

157. Undaunted, the groundbreaking research done by Dr. Gurbel and others continued after 2006. *See* J.L. Mega, *et al.*, *Cytochrome P-450 Polymorphisms and Response to Clopidogrel*, 260 N. ENGL. J. MED. 354-62 (2009); J.M. Sweeny, *et al.*, *Antiplatelet drug 'resistance'. Part 1: mechanisms and clinical measurements*, 6 NAT. REV. CARDIOL. 273-82 (2009); F. Sofi, *et al.*, *Cytochrome P450 2C19*2 polymorphism and cardiovascular recurrences in patients taking*

24 [redacted]
25

clopidogrel: a meta-analysis, 11 PHARMACOGENOMICS J. 199-206 (2011) ("significant association between the CYP2C19*2 polymorphism and an increased risk of major adverse cardiovascular events in the follow-up");

158. The Shuldiner-Gurbel study published in 2009 also estimated that the CYP2C19*2 loss-of-function allele is even more common among African-American (~33% with at least one copy) and Asian (~51% with at least one copy) populations. *See* A. Shuldiner, *et al., Association of Cytochrome P450 2C19 Genotype with the Antiplatelet Effect and Clinical Efficacy of Clopidogrel Therapy,* 302 JAMA 849-58 (2009). Defendants themselves had noted that [redacted] ".[26]

159. Based on the foregoing studies by Dr. Gurbel and others, there was a small, but growing body of evidence suggesting the effectiveness of Plavix depends on activation to an active metabolite by the cytochrome P450 (CYP) system, principally CYP2C19, and that poor metabolizers treated with Plavix at FDA-approved doses exhibit higher cardiovascular event rates following acute coronary syndrome ("ACS") or percutaneous coronary intervention ("PCI") than patients with normal CYP2C19 function.

160. Unfortunately, it was not until December 2008 when *the FDA first notified Defendants* of "new safety information" that it believed should be included in the labeling for Plavix. When it approved labeling changes in 2009, the FDA wrote to Defendants:

> This information pertains to the risk addressed in several published reports describing the metabolic pathway of clopidogrel in vivo, investigating factors involved in the bioavailability of its active metabolite, and reporting an increased reporting rate of cardiovascular ischemic events in poor responders to Plavix (clopidogrel bisulfate).

[26] [redacted]

By this point, of course, this "new safety information" had been available to Defendants since at least [redacted], and it should have been Defendants that updated the product labeling to provide "adequate instructions" to use Plavix safely and effectively, and alerted the FDA and the medical community of this information, and not the other way around. Instead, Defendants' strategy was to "[redacted]",[27] thereby jeopardizing the health of millions of Americans at the expense of the American taxpayer.

C. DEFENDANTS' FAILURE TO TIMELY NOTIFY PHYSICIANS OF ADVERSE EFFICACY DATA FOR PLAVIX PUT PATIENTS AT RISK

161. Defendants' failure to timely update its Plavix labeling to provide physicians with "adequate instructions" to use the drug safely and effectively, failure to notify physicians of adverse efficacy data for Plavix, and Defendants' false and misleading promotion, put patients at risk. Even as early as 2004, although studies had not yet identified CYP2C19 as an important culprit, they had clearly identified the low responder issue and linked it to adverse clinical outcomes. Defendants were acutely [redacted][28] but did everything possible to avoid telling physicians the truth and to avoid further studies that would dig deeper into this issue.

162. These early studies were cited in the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention. Of particular note, the Guidelines state:

> Preliminary data suggests that clopidogrel "nonresponders" may be at higher risk for thrombotic events. Thus, in patients in whom stent thrombosis may be catastrophic or lethal (ULM, bifurcating left main, and last patent coronary vessel), platelet aggregation studies may be considered and the dose of clopidogrel increased to 150 mg per day if less than 50% inhibition of platelet aggregation is demonstrated.[29]

[27] [redacted]

[28] [redacted]

[29] Smith, *et al.*, *ACC/AHA/SCAI Practice Guidelines*, at 64 (2005) (available at http://www.acc.org).

163. [redacted][30] [redacted]"[31] In other words, Defendants simply doubled-down on their efforts to misinform physicians that there were no contraindications, and that Plavix should be used on all patients needing platelet inhibition therapy.

164. Although Defendants' efforts bought them a decade of full-throttle marketing, finally additional independent scientific studies began to reveal the full truth.

165. For example, a study published in the NEW ENGLAND JOURNAL OF MEDICINE in January 2009 concluded:

> Among patients with an acute myocardial infarction who were receiving [Plavix], those carrying the CYP2C19 loss-of-function alleles had a higher rate of subsequent cardiovascular events than those who were not. This effect was particularly marked among the patients undergoing percutaneous coronary intervention.

See T. Simon, *et al*., *Genetic Determinants of Response to Clopidogrel and Cardiovascular Events*, 360 N. ENGL. J. MED. 363-75 (2009).

30 [redacted]

31 *Id.*

166. Similarly, in January 2009 THE LANCET published a study that examined 259 patients who survived a first myocardial infarction and were treated with Plavix for at least a month in order to assess whether the CYP2C19*2 polymorphism affected long-term prognosis of patients who were chronically treated with Plavix. The authors concluded:

> [O]ur study shows a strong relation between the presence of the CYP2C19*2 allelic variant and recurrent thrombotic coronary events in clopidogrel-treated patients predominantly of European ancestry who survived a myocardial infarction before 45 years of age.

J-P. Collet, *et al*., *Cytochrome P450 2C19 polymorphism in young patients treated with clopidogrel after myocardial infarction: a cohort study*, 373 THE LANCET 309-17 (2009).

167. Others had reached similar conclusions regarding the relative safety of treating CYP2C19*2 carriers with Plavix. *See, e.g.*, D. Sibbing, *et al*., *Cytochrome P450 2C19 loss-of-function polymorphism and stent thrombosis following percutaneous coronary intervention*, 30 EUR. HEART J. 916-22 (2009) ("CYP2C19*2 carrier status is significantly associated with an increased risk of [stent thrombosis] following coronary stent placement."); B. Giusti, *et al*., *Relation of cytochrome P450 2C19 loss-of-function polymorphism to occurrence of drug-eluting coronary stent thrombosis*, 103 AM. J. CARDIOL. 806-11 (2009) ("The present study provided the novel finding that the 2C19*2 allele of the CYP2C19 gene was an independent risk factor for drug-eluting [stent thrombosis]."); A. Shuldiner, *et al*., *Association of Cytochrome P450 2C19 Genotype with the Antiplatelet Effect and Clinical Efficacy of Clopidogrel Therapy*, 302 JAMA 849-58 (2009).

168. Indeed, large meta-analyses have shown that CYP2C19*2 carriers (both one and two loss of function allele patient) treated with Plavix have a higher risk for major adverse cardiovascular events as opposed to non-carriers and higher risks of stent thrombosis. *See* Mega, J., *et al., Reduced-Function CYP2C19 Genotype and Risk of Adverse Clinical Outcomes Among*

Patients Treated with Clopidogrel Predominantly for PCI: A Meta-Analysis, 304 JAMA 1821-1830 (2010) (among 9865 patients, a significantly increased risk of the composite endpoint was evident in both carriers of one (HR 1.55, 95% CI 1.11-2.27, P=0.01) and two (HR 1.76, 95% CI 1.24-2.50, P=0.002) *CYP2C19* reduced-function alleles).

169. These studies document the human cost of Defendants' failure to provide physicians with timely "adequate instructions" to use Plavix safely and effectively, a failure that was an integral tactic in Defendants' scheme to elevate profits over people—largely at the expense of the United States taxpayers.

D. DEFENDANTS' CONTROL OF DESIGN, ANALYSIS, AND PUBLICATION OF PLAVIX CLINICAL TRIALS IN PEER-REVIEWED MEDICAL JOURNALS

170. Even though smaller studies in the clinical literature had begun to disclose the nature and extent of the non-responder issue, Plavix remained for many physicians and hospitals the standard of care for treating all antithrombotic and antiplatelet patients. This is not surprising given that Defendants' exercise of control over Plavix clinical trials would successfully limit awareness of the issue.

171. Leading physicians rely on the findings of published studies in respected peer-reviewed medical journals to make the best decisions for their patients. However, Defendants' corporate influence concerning Plavix studies had permeated every aspect of the research process including: the design of clinical studies (including the trial population, the choice of drugs, doses, duration of the trial, and the outcome and safety measures to be tracked); control of the data and data analysis; ghost-writing the manuscripts for articles, and publication decisions (including where, or even whether the study will be published); and publicity following publication.

172. As the National Institute of Health ("NIH") funding of clinical trials started decreasing in the late 1970s, pharmaceutical companies like Defendants moved in to fill the void.

Between 1977 and 1990, pharmaceutical companies increased their funding for clinical trials six-fold.[32] By 1991, approximately 70% of clinical trials were being funded by the pharmaceutical companies, but 80% of those trials were still being carried out in academic medical centers where there was a tradition of academic researchers participating in study design, data analysis and publication decisions.[33] As the 1990s progressed, this changed dramatically, so that by 2000 only 41% of commercially funded studies were being done in universities; the rest were being done by for-profit contract research organizations. By 2004, only 26% of commercially funded studies were being performed in an academic setting.[34]

173. One important consequence of this transition with regard to Plavix research is that it has changed the locus of control of clinical research from academic researchers working in academic medical centers to the pharmaceutical company Defendants themselves. Since Defendants were hiring the research companies directly, they played the primary role in designing most Plavix studies and controlling the data, while at the same time denying researchers like Dr. Gurbel, who would author the articles to be published in medical journals (the "scientific evidence"), free access to the data. This has allowed Defendants to retain a great deal of control over the Plavix publication decisions.

174. As of 2006, eighty to ninety percent of clinical research was commercially funded by drug company sponsors like Defendants. In the ten years between 1994 and 2003, sixty-five of the seventy-seven most frequently cited clinical trials, or 84%, had commercial sponsorship.

[32]Dramatic Growth of Research and Development, Pharmaceutical Research and Manufacturers of America (PhRMA), *Pharmaceutical Industry Profile 2003* (2003). http://www.phrma.org/publications/publications/profile02/2003%20CHAPTER%202.pdf.
[33]Bodenheimer, *Uneasy alliance – clinical investigators and the pharmaceutical industry*, 342 NEJM 1539-1544 (2003).
[34]Steinbrook, *Gag Clauses in Clinical-Trial Agreements*, 352 NEJM 2160-62 (2008).

Furthermore, the percentage increased significantly during that time: since 1999, thirty-one out of thirty-two of the most frequently cited clinical trials, or 97%, had industry sponsorship.[35]

175. A study published in the NEW ENGLAND JOURNAL OF MEDICINE ("NEJM") examined the standards for the arrangements between pharmaceutical companies and academic medical centers—the clinical trial contracting agreements that would be expected to maintain the highest standards of academic independence. The researchers found that more than two-thirds of the academic institutions accepted research contracts that prohibited researchers from changing the sponsor's research design. Half of the university medical centers allowed commercial sponsors like Defendants to "draft manuscripts reporting the research results, with the investigators' role limited to review and suggestions for revision." And "24 percent of the responding institutions would grant the sponsor the right to insert its own statistical analyses into manuscripts."[36]

176. Discussing the failure of universities to defend their scientists' research independence when conducting commercially-sponsored medical studies, Drummond Rennie, MD, Deputy Editor of the JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION ("JAMA"), said that universities and scientists "are seduced by industry funding, and frightened that if they don't go along with these gag orders, the money will go to less rigorous institutions…. It's a race to the ethical bottom."[37]

177. Sadly, given the primary fiduciary responsibility that Defendants had to their shareholders rather than the public's health, this transition from public to private financing of

[35]Patsopoulos, *et al*., *Origin and funding of the most frequently cited papers in medicine: database analysis*, 332 BMJ 106-64 (2006).
[36]Mello, *et al*., *Academic medical centers' standards for clinical-trial agreements with industry*, 352 NEJM 2202-10 (2005).
[37] Knox, BOSTON GLOBE, March 30, 1999.

Plavix clinical research has meant that, at best, studies have maximized Defendants' corporate profits rather than optimizing health most effectively and efficiently.

178. As of 2005, between two-thirds and three-quarters of the clinical studies published in even the most prestigious journals were commercially funded.[38] Among the highest quality published studies (those deemed good enough to be included in Cochrane Reviews), the odds were 5.3 times greater that commercially funded studies would conclude that the sponsor's drug was the treatment of choice compared to non-commercially funded studies of exactly the same drugs.[39] With regard to Plavix, this meant that the "scientific evidence" produced by commercially sponsored studies was very likely to be biased in favor of Defendants. An editorial in the AMERICAN JOURNAL OF MEDICINE noted that the "link between commercial sponsorship and the conduct and presentation of research" is difficult to minimize "because there is usually a substantial power gradient between the sponsor and the investigator."[40]

179. Defendants also successfully biased even the most trusted "scientific evidence" by having financial relationships with researchers, funding research and coordinating research publications, or (as alleged below) refusing to fund research. A study of the effect of researchers' financial conflicts of interest and industry funding on clinical trials, published in the AMERICAN JOURNAL OF PSYCHIATRY in 2005, concluded: "Industry sponsorship and author conflict of interest are prevalent and do appear to affect study outcomes."[41] The study looked at clinical trials that were published between 2001 and 2003 in the four most widely cited general psychiatry journals.

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[38] Smith, *Medical Journals Are an Extension of the Marketing Arm of Pharmaceutical Companies*, 2(5) PLOS MEDICINE 138 (2005), available at 10.1371/journal.pmed.0020138.
[39] Als-Neilsen, et al., *Association of Funding and Conclusions in Randomized Drug Trails*, 290 JAMA 921-28 (2003).
[40] Landefeld, *Commercial Support and Bias in Pharmaceutical Research*, 117 AM J MED 876-78 (2004).
[41] Perlis, *et al*., *Industry Sponsorship and Financial Conflict of Interest in the Reporting of Clinical Trials in Psychiatry*, 162 AM J PSYCHIATRY 1957-60 (2005).

Forty-seven percent of the articles included at least one author with a financial conflict of interest, defined as "any report of consulting or speaking fees or honoraria, stock ownership, or employment by the study sponsor." The odds were 4.9 times higher that articles including at least one author with a conflict of interest would report positive results for the drug company's product. For those studies that had both industry sponsorship and at least one author with a conflict of interest the odds were 8.4 times higher than the study would favor the sponsor's drug.

180. In short, Defendants exploited this system to produce "scientific studies" that publicly obscured and diminished what it had known privately since [redacted], and thereby provided cover for its knowing failure to abide by its legal obligation to update the Plavix labeling so as to provide physicians with "adequate instructions" to use the drug safely and effectively.

E. DEFENDANTS' SIN WAS THUS NOT MERELY ONE OF OMISSION, BUT ALSO ONE OF COMMISSION

181. Meanwhile, Defendants directed their sales forces (including sales representatives like Ms. Evans) to tell physicians that they were providing them with all the pertinent data for Plavix, even as they withheld the unfavorable data regarding diminished (or no) responsiveness. This put patient lives at risk because Defendants effectively encouraged physicians to recommend therapies and procedures based on the false belief that Plavix would provide adequate antithrombotic and antiplatelet protection for all of their patients. For example, Defendants encouraged Dr. Stahl to believe that Plavix was an appropriate therapy for virtually his entire antithrombotic and antiplatelet patient population without need for any platelet function or genetic testing, and that to the extent patients were not responding to therapy, their non-responsiveness was due to patient non-compliance (*i.e.*, not taking the drug as prescribed) or dosing (*i.e.*, not taking enough of the drug).

182. Defendants actively encouraged tens of thousands of physicians, including Dr. Stahl, to prescribe Plavix based on what Defendants knew to be their false and misleading representation that all antithrombotic and antiplatelet patients would benefit. Had physicians known that over 30% of patients would have diminished (or no) responsiveness to Plavix, they would not have recommended drug-eluting stents as broadly as they did because patients who receive such stents are highly dependent on antithrombotic and antiplatelet agents, such as Plavix, to prevent catastrophic clotting in the stent.

183. Had physicians been properly informed that Plavix was ineffective on over 30% of the patient population, they would have treated them differently. Rather than prescribing a contraindicated, and therefore medically unnecessary and unreasonable, drug that worked no better than a placebo, to begin with, physicians would have immediately recognized the need to conduct platelet aggregation testing before prescribing Plavix or, if Plavix had been administered in an emergency treatment setting, to conduct platelet aggregation testing afterward. While quick bedside platelet aggregation testing did not come to the market until mid-2005, several research laboratory methods that determine the extent of platelet inhibition in patients, either at baseline or after any antiplatelet therapy, had been available for decades in many hospitals.

184. Defendants' hostility toward testing included its use as a diagnostic tool by physicians, as reflected by efforts to confuse and obfuscate the facts concerning available testing. For example, [redacted].[42]

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[42] [redacted].

185. By way of further example, in [redacted], shortly after the Accumetrics VerifyNow platelet aggregation test began to be marketed ([redacted]),[43] Defendants [redacted].[44]

186. Internally, Defendants repeatedly acknowledged the [redacted],[45] [redacted],[46] [redacted]

187. Such a position was spurious at best, given the fact platelet function testing data had been precisely the basis for the 1997 FDA approval of clopidogrel as a platelet inhibitor.[47] And any lack of adequately powered trials linking testing and adverse clinical outcomes had largely been the result of [redacted] Moreover, Defendants knew of [redacted]

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43 [redacted].

44 [redacted].

45 [redacted]

46 [redacted] (underlining in original).

47 *See* http://www.accessdata.fda.gov/drugsatfda_docs/nda/97/20839_Plavix_clinphrmr_P1.pdf at 2, 9; http://www.accessdata.fda.gov/drugsatfda_docs/nda/97/20839_Plavix_clinphrmr_P2.pdf; http://www.accessdata.fda.gov/drugsatfda_docs/nda/97/20839_Plavix_appltr_prntlbl_medr_chemr_EA_phrmr.pdf.

[redacted])[48] [redacted]

188. The reason for Defendants' hostility toward platelet function testing was that they knew it would reveal [redacted],[49] [redacted].[50] In short, for over 30% of patients the drug was contraindicated and therefore essentially a medically unnecessary and unreasonable placebo.

189. But Defendants feared that [redacted] since it would not be medically reasonable or necessary for physicians to prescribe a placebo. For example, in [redacted] Defendants discussed [redacted]

[48] [redacted]

[50] [redacted]

[redacted]."[51] Three years later, with platelet aggregation tests rapidly becoming available and Effient on the verge of launch, [redacted].[52]

190. Defendants' hostility toward testing was also a long-standing basis for refusing to support various clinical studies. For example, on [redacted], Defendants' [redacted]."[53] This hostility toward the inclusion of testing in clinical trials continued unabated for years.

191. In [redacted], there was considerable [redacted]"[54] Attacks on that idea included [redacted]."[55]

192. Once public research appeared showing that Plavix responsiveness may be largely dependent upon the normal functioning of the CYP2C19 liver enzyme, Defendants' hostility toward testing as a diagnostic tool took a new turn. While there was at the time a commercially available DNA blood test to establish definitively whether a patient has the CYP2C19 gene

51 [redacted]
52
53
54
55

polymorphisms associated with abnormal Plavix responsiveness, Defendants did not embrace it. [redacted].

193. Defendants also continued their hostility toward the commercially available assay developed by Accumetrics, the VerifyNow $P2Y_{12}$. This FDA-approved, simple bedside blood test determines the extent of platelet inhibition in patients on a thienopyridine, such as Plavix. The results, reported as platelet response units (PRU), are available immediately and therefore can be factored into the clinical decision making process. This test has been available since September 2005. Multiple studies have shown that residual platelet responsiveness (PRU greater than 208) is significantly correlated with adverse clinical outcomes in PCI-stent patients.

194. However, by failing to provide timely "adequate instructions" to use Plavix safely and effectively, and withholding critical efficacy data from the FDA and physicians, Defendants impacted how physicians treated their patients, influencing them to make bad decisions and recommendations to the ultimate detriment of patient safety, and at great direct and indirect cost to taxpayers. Due in part to Defendants' failure to timely update the Plavix label to provide physicians with "adequate instructions" to use the drug safely and effectively, and to report adverse efficacy data to physicians and to the FDA, all as it was required to do, it was not until May 2009 that (based on the FDA's initiative) Defendants obtained FDA-approval of a revised label for Plavix that expressly addressed the fact that, due to polymorphisms in the CYP2C19 enzyme, not all patients taking Plavix will have adequate platelet inhibition.

195. Later in 2009, the FDA required that Defendants add a "WARNINGS" section to the label that specifically described the potential for reduced effectiveness of Plavix due to impaired CYP2C19 function.

196. And in March 2010, the FDA required that Defendants add a "Black Box Warning" to the label for Plavix, specifically alerting physicians and patients as follows:

WARNING: DIMINISHED EFFECTIVENESS IN POOR METABOLIZERS ***See full prescribing information for complete boxed warning.***
• **Effectiveness of Plavix depends on activation to an active metabolite by the cytochrome P450 (CYP) system, principally CYP2C19. (5.1)** • **Poor metabolizers treated with Plavix at recommended doses exhibit higher cardiovascular event rates following acute coronary syndrome (ACS) or percutaneous coronary intervention (PCI) than patients with normal CYP2C19 function. (12.5)** • **Tests are available to identify a patient's CYP2C19 genotype and can be used as an aid in determining therapeutic strategy. (12.5)** • **Consider alternative treatment or treatment strategies in patients identified as CYP2C19 poor metabolizers. (2.3, 5.1)**

197. Today, armed with accurate information about Plavix, Dr. Stahl routinely sends his patients for platelet reactivity testing before treating them with a stent, as well as during treatment, in order to determine whether they possess the genetic predisposition to low- or non-responsiveness to Plavix. Through this protocol, he is finding that as many as thirty to forty percent (30% - 40%) of his patients, including those who have been on long-term therapy with Plavix, are low- or non-responders—a sobering observation since it suggests that, due to Defendants' misconduct, a significant number of his (and other physicians') patients were placed at risk—in essence receiving a placebo.

198. By failing to timely and proactively comply with their legal obligation to update the Plavix label to provide physicians with "adequate instructions for use," and to alert the FDA and physicians to the fact that a significant portion of the population was genetically predisposed

to diminished or non-responsiveness to Plavix, Defendants unnecessarily placed patients at risk. Had physicians been fully and timely informed not just that a significant segment of the population would have diminished (or no) response to Plavix, but also that tests were available to determine each patient's genetic predisposition, physicians could have designed alternate therapy regimens that would have been more effective and safer for their patients, and prevented the expenditure of hundreds of millions of taxpayer dollars.

199. While patient safety was the primary victim of Defendants' failure to disclose adverse efficacy data and Defendants' subsequent improper effort to counteract that data, patients, Government Purchasers and Government Programs also paid a hefty economic price for Defendants' misconduct.

200. Defendants knew that, if the FDA and medical community were fully informed that over 30% of the patient population was genetically predisposed to have diminished or no response to Plavix, then physicians would have treated those patients using alternate therapies instead of Plavix. *See, e.g.*, A. Shuldiner, *et al*., *Association of Cytochrome P450 2C19 Genotype with the Antiplatelet Effect and Clinical Efficacy of Clopidogrel Therapy*, 302 JAMA 849-58 (2009) ("Those with the CYP2C19*2 genotype may benefit more from an antiplatelet regimen that does not include [Plavix], such as the third-generation thienopyridine prasugrel, or ticagrelor and cangrelor."). Even Dr. Deepak Bhatt, principal investigator for the Defendant-funded CHARISMA trial, opined in 2009 that:

> Beyond merely identifying risk, the major reason to perform pharmacogenomic testing [for the CYP2C19 polymorphism] would be to identify patients in whom an alternative antiplatelet approach would decrease ischemic events.

Deepak L. Bhatt, *Tailoring Antiplatelet Therapy Based on Pharmacogenomics*, 302 JAMA 896-97 (2009). Of course, if that alternate approach did not include Plavix, the negative effect on Defendants' sales and revenue could have been dramatic.

201. By failing to timely update the Plavix label with "adequate instructions for use" to disclose adverse efficacy data for Plavix, and by subsequently misrepresenting that data, Defendants caused patients and their benefit plans to pay for vast quantities of a drug that Defendants *knew* would be contraindicated and therefore medically unnecessary and unreasonable for over 30% of the patient population.

202. Similarly, Defendants knew from the outset that a significant percentage of patients treated with Plavix were, and would be, Government Program beneficiaries. For example, approximately 30% of Dr. Stahl's patients are Medicare beneficiaries. By failing to timely disclose adverse efficacy data for Plavix, and by subsequently misrepresenting that data, Defendants caused Government Programs to reimburse payments for vast quantities of a drug that Defendants *knew* would be ineffective for this patient population.

203. Defendants compounded the financial harm to Government Purchasers and Government Programs when they sought to counteract publicity regarding diminished responsiveness to Plavix by proactively encouraging physicians to *over-prescribe* the drug, using dosing regimens that exceeded the dosing regimen set forth in the FDA label. This, too, caused financial harm by forcing payors to purchase unapproved—and quite possibly still ineffective—quantities of the drug. Moreover, as the FDA label for Plavix explains that there are significant adverse reactions associated with Plavix, including life-threatening and fatal bleeding, which would be exacerbated by the overdosing that Defendants recklessly promoted. Indeed, the FDA label specifically warns that an overdose of Plavix "may result in bleeding complications."

VI. DEFENDANTS' SCHEME TO DECEIVE GOVERNMENT PROGRAMS AND GOVERNMENT PURCHASERS

204. From at least as early as [redacted], Defendants knew that a significant percentage of patients were genetically predisposed to have substantially diminished or no responsiveness to

Plavix. Defendants were required by law to update the labeling and disclose this information to the FDA, but failed to do so because they knew that disclosure would lead to a reduction in the number of prescriptions written for Plavix and, consequently, a significant decline in profits.

205. Defendants knew that, if the FDA and medical community were fully informed that over 30% of the population was genetically predisposed to have diminished or no response to Plavix, then physicians would treat those patients using alternate therapies instead of Plavix. Despite having this knowledge, Defendants did not alert physicians to the drug's diminished effectiveness in non-responders for whom Plavix was contraindicated and therefore essentially a medically unnecessary and unreasonable placebo.

A. THE FRAUDULENT "[redacted]" CONCEALMENT SCHEME

206. Pursuant to Defendants' deceptive "[redacted]" scheme to conceal the fact the Plavix defect ("Fraudulent '[redacted]' Concealment Scheme"), Defendants failed to disclose—as the law requires (*see* 21 C.F.R. § 314.80)—adverse efficacy data that demonstrates for over 30% of Plavix patients the drug was contraindicated and therefore essentially a medically unnecessary and unreasonable placebo. The FDCA also required Defendants to update the Plavix label to ensure "adequate instructions" to use Plavix safely and effectively. As alleged below, Defendants' conduct put patients at risk, and caused patients, Government Purchasers and Government Programs to pay significant sums for drugs that offered little more than a placebo effect, if that.

207. Post-FDA approval of Plavix in 1997, Defendants soon learned that there was credible evidence non-responders would receive little, or no, clinical benefit from Plavix.

208. [redacted]. The [redacted]

[redacted]

Defendants failed to update the drug's labeling, or to notify the FDA, physicians or patients of this potential non-responder risk.

209. From the outset, it was clear Defendants had little interest in funding research which might threaten sales of Plavix. Defendants' awareness of the importance of CYP2C19, and awareness that CYP2C19 polymorphisms were likely one of the key causes of low responsiveness, did not result in a drive to find the truth and assist physicians in delivering the best health care for patients. Instead, driven by the enormous profits they were reaping from Plavix sales, Defendants sought to prevent studies that might reveal the CY2C19 issue, or otherwise focus scientific attention on the genomics (*i.e.*, the polymorphisms) of the enzymes involved in Plavix oxidation. Defendants achieved this objective by refusing to fund studies, controlling study designs, and/or controlling the analytical methods used.

210. The culprit in the "[redacted]" scheme was the [redacted]

[redacted]

56 [redacted]

57 [redacted]

[redacted].[58] Rather than fostering scientific research concerning Plavix, [redacted]

[redacted].

211. [redacted]

[redacted].[59]

[redacted].„[60] [redacted]

[redacted].

212. [redacted]

[redacted][61]

213. [redacted]

[redacted]

58 [redacted]
59
60
61

[redacted].[62]

214. That the profit motive was the guiding [redacted].[63]

215. [redacted].”[64]

216. [redacted].[65]

217. [redacted],[66] [redacted]

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62 [redacted]
63
64
65
66

[redacted][67].

218. [redacted]

[redacted][68]

219. [redacted]

[redacted].,,[69] [redacted]

220. [redacted]

67 [redacted]
68
69

[redacted]

[redacted]”[70]

221. [redacted]

[redacted]

[redacted]

[redacted][71] [redacted]

[redacted]”[72]

222. [redacted]

[redacted]

[redacted][73] [redacted]

[redacted]”[74] [redacted]

[redacted]

[redacted]

[redacted]

70 [redacted]

71

72

73

74

223. [redacted]"[75],

[redacted]

[redacted]

[redacted]

224. [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

225. [redacted]

[redacted]

[redacted]

[redacted][76].

[75] [redacted]

[76] [redacted]

226. [redacted].[77] [redacted].[78]

227. [redacted].”[79]

228. [redacted]

77 [redacted]
78
79

[redacted] ,,80

229. [redacted]

[redacted] 81

230. [redacted]

[redacted] ,,82

231. [redacted]

80 [redacted]
81
82

[redacted]

[redacted]:

[redacted]

[redacted]

[redacted][84].

232. [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[83] [redacted]

[84] *Id.*

[redacted]."[85]

233. [redacted]"[86]

234. [redacted]."[87]

235. [redacted]

---

85 [redacted]

86 [redacted]

87 [redacted].

[redacted][88]

236. [redacted][89]

237. [redacted],,[90]

238. [redacted][91]

88 [redacted]

89 [redacted].

90 [redacted]

91 [redacted]

[redacted].”[92]

[redacted].[93]

239. [redacted]

[redacted].” [94] [redacted]

[redacted].[95]

240. [redacted]

[redacted].”[96] [redacted]

[redacted]:

[92] *Id.*

[93] [redacted].

[94]

[95]

[96]

[redacted]

[redacted].”[97]

241. Finally, only when the FDA came knocking did Defendants begin to concede internally that there were issues with clopidogrel responsiveness. Based on the series of publications on CYP2C19 polymorphism and the Plavix non-responder issue, the FDA contacted Defendants on December 5, 2008 to request an “[redacted].”[98]

242. [redacted]

[redacted].”[99] At no time, however, did Defendants disclose to the FDA that, as early as their [redacted] they not only had VOR data which had never been communicated, they had known about this issue for [redacted].

243. [redacted]

[redacted].”[100]

244. [redacted]

97 [redacted]

98 [redacted]

99 [redacted]

100 [redacted].

[redacted] ,,101 [redacted] ,,102 [redacted] ,,103

245. The FDA rejected Defendants' proposal to continue to study the non-responder issue and in October 2009 required instead the following language be inserted into the Plavix Warnings section regarding "reduced effectiveness due to impaired CYP2C19 function":

- "Avoid use of Plavix in patients with impaired CYP2C19 function due to known genetic variation or due to drugs that inhibit CYP2C19 activity."
- "Genetic variations: Patients with genetically reduced CYP2C 19 function have diminished antiplatelet responses and generally exhibit higher cardiovascular event

101 [redacted]
102 [redacted]
103 [redacted]

rates following myocardial infarction than do patients with normal CYP2C19 function."[104]

246. [redacted]."[105]

[redacted][106] [redacted]

[redacted]"[107]

247. The FDA did not agree. The following year in March 2010 the FDA required that the Black Box Warning be included in the Plavix package insert advising healthcare professionals that patients who are poor metabolizers of PLAVIX exhibit higher cardiovascular event rates than patients with normal CYP2C19 function, at recommended doses.

248. Even while Defendants were still engaged in delay and obfuscation, insisting all the while that Plavix was safe and effective for all ACS patients, there were thousands of adverse events reported to the FDA via its MedWatch system that Plavix had been ineffective, including numerous reports of adverse events for non-responders (including many Government Program-eligible patients), such as:

104 [redacted]
105
106
107

- **MedWatch Report No. A03200800853 dated December 4, 2008.** "[redacted]"[108]
- **MedWatch Report No. A03200803456 dated December 4, 2008.** "[redacted]"[109]
- **MedWatch Report No. 2010SA004782 dated December 29, 2010.** "[redacted]"[110]
- **MedWatch Report No. 2010SA005832 dated December 29, 2010.** "[redacted]

108 [redacted].
109 [redacted].
110 [redacted]

[redacted]

[redacted]

[redacted].”[111]

- **MedWatch Report No. 2009SA00B789 dated December 29, 2010.** “[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]”[112]

- **MedWatch Report No. 2010SA034427 dated December 29, 2010.** “[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]”[113]

- **MedWatch Report No. 2010SA038664 dated December 29, 2010.** “[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]”[114]

111 [redacted]
112
113
114

B. THE FRAUDULENT "EXPAND AND PROTECT" MARKETING SCHEME: DEFENDANTS PRIORITIZED PROFITS OVER PATIENT HEALTH CARE

249. As alleged herein, Defendants have systematically and deliberately promoted Plavix through false and misleading advertising that overstated efficacy, and minimized critical adverse event and risk information. Defendants would brand this their "Expand and Protect" strategy[115] (formerly from at least 2004 to 2007, its "[redacted]"[116] strategy and from 2007-2009 its "[redacted]"[117] strategy). The key to protecting Plavix would be to sell its safety and efficacy in all patients, in spite of the fact that [redacted] had shown otherwise. The "Expand & Protect" message became so ubiquitous that [redacted]

[redacted]

250. Defendants' motive to ignore the law repeatedly and put patient safety at risk has been money. Plavix has been a financial blockbuster drug for Defendants. Even though in 1997 Defendants had only forecast its annual U.S. sales to reach $[redacted] per year,[118] by any measure, Plavix has been a blockbuster with total sales worldwide between 1997 and 2012, according to Forbes, reaching $74 billion.[119]

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115 [redacted]

116 [redacted]

117 [redacted].

118 [redacted]

119 King, *The Best Selling Drugs Since 1996 - Why AbbVie's Humira Is Set To Eclipse Pfizer's Lipitor*, FORBES (July 15, 2003), available at http://www.forbes.com/sites/simonking/2013/07/15/the-best-selling-drugs-since-1996-why-abbvies-humira-is-set-to-eclipse-pfizers-lipitor/#2609a0d22055 (last checked on Jan. 16, 2017).

251. The overriding profit motive is evident from internal documents reflecting Defendants' knowledge that [redacted]

252. [redacted][120] [redacted].[121] [redacted] [122] [redacted]

253. [redacted].[123]

254. [redacted]

[120] [redacted]
[121] *Id.*
[122] *Id.*
[123] [redacted]

[redacted].[124] [redacted]

255. [redacted].[125]

256. [redacted]."[126] [redacted]"[127]

257. [redacted].[128]

258. [redacted]

---

124 [redacted]

125 [redacted]

126 [redacted]

127 [redacted].

128 [redacted]

[redacted] ,,[129]

259. [redacted]

[redacted] [130] [redacted]

260. [redacted]

[redacted] [131]

261. [redacted]

129 [redacted]

130

131

[redacted] [132].

262. [redacted] [133] [redacted] [134]

263. [redacted] [135].

264. [redacted] [136].

132 [redacted].

133 [redacted]

134 [redacted].

135 [redacted].

136 [redacted]

265. [redacted][137] [redacted][138] [redacted][139]

266. [redacted][140] [redacted][141]

137 [redacted]
138
139
140
141

[redacted].[142]

267. In July 2007, Defendants launched a new marketing initiative, the [redacted] It became a marketing "[redacted]" to "[redacted]" the competition by encouraging "[redacted]" doses of Plavix for *all* ACS heart attack patients, including in hospital emergency rooms prior to surgery, "[redacted]."[143] Once the patient was on Plavix in the ER, Defendants knew it would be unlikely they would be switched to another antiplatelet drug in the cath lab.[144]

268. [redacted], [145] [redacted]. [146]

269. [redacted]."[147] [redacted]."[148] [redacted]

142 [redacted]
143
144
145
146
147
148 *Id.*

[redacted]

[redacted][150]

270. [redacted]

[redacted][151] [redacted]

[redacted]

149 [redacted]
150
151

271. To ensure that sales representatives around the United States followed through with the message, managers were to (and did) [redacted].[152]

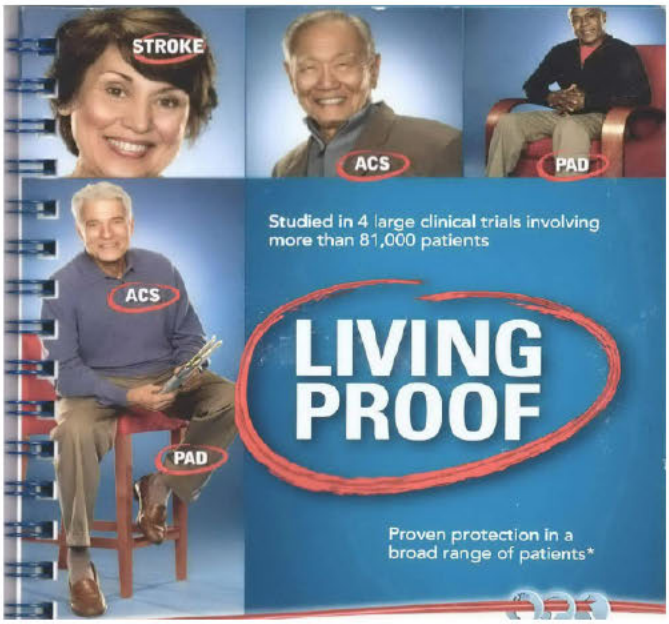
272. As early as 2007, Sanofi and BMS sales representatives had been trained that clinical studies demonstrated that rates of diminished response were higher among African-Americans and Asian-Americans. They were told that African-Americans and Asian-Americans were less likely to benefit fully from Plavix. Defendants showed them clinical studies demonstrating the extent of the problem among specific ethnic subcategories.

273. However, during their promotional details and programs, sales representatives and company speakers were not to not discuss the cytochrome P450 issue unless it was raised by a physician, in which case they were permitted to respond to the inquiry by directing the physician to speak with a medical science liaison who would provide the scripted response that there was inadequate clinical research demonstrating a correlation between non-response and outcomes and that the problem (if it existed at all) was limited to a very small population.

274. In 2008, Defendants began their "Living Proof" marketing campaign, which provided examples of specific patient types for whom Plavix was effective along with the deceptive tagline "Proven protection in a broad range of patients." Defendants' 2008 "Living Proof" marketing materials provided to Evans and her Plavix sales representative colleagues included cue cards detailing pictures of actors portraying representative patients who were good candidates for using the drug. Even though Defendants were aware from [redacted] and the published literature that Asian-Americans and African-Americans had a greater propensity to be poor metabolizers, Defendants' 2008 "Living Proof" detail piece prominently

[152] [redacted]

featured Asian-American and African-American actors as patient examples where Plavix had been "proven" effective:



275. The "Living Proof" campaign aimed at getting the message out about the "proven efficacy and well established safety profile" of Plavix "in a broad range of patients." [redacted][153].

276. [redacted][154].

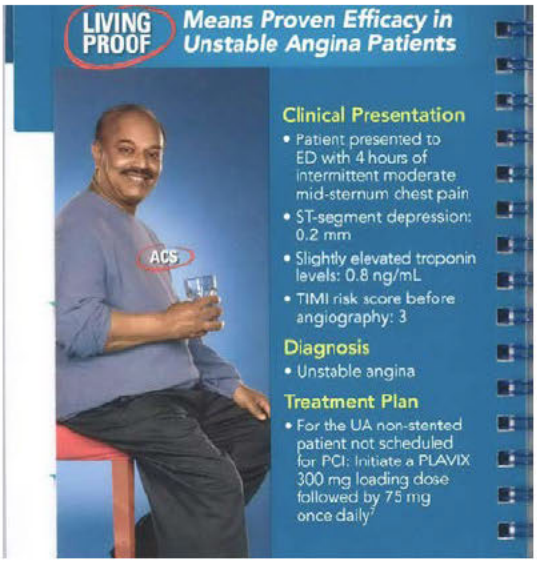
153 [redacted]
154

[redacted]

[redacted]"[155] The sales representatives were to (and did) use this [redacted] patient type for ACS patients as "[redacted]" despite the fact that they were aware that [redacted] had a significantly higher propensity to be non-responders.

277. One of the patient examples in the 2008 "Living Proof" Plavix marketing materials was an overweight African-American male who had suffered from unstable angina with the claim that "Living Proof: Means Proven Efficacy in Unstable Angina Patients" with no warning at all that African-Americans were at a greater risk of a poor clopidogrel response:

[155] [redacted]



278. Even after the FDA had mandated a change in the Plavix label, the 2009 detail piece Defendants used to sell Plavix nonetheless still included the example of a 58-year-old named "Henry," an overweight African-American male who had peripheral artery disease,[156] again with no warning at all that African-Americans were at a greater risk of a poor clopidogrel response. Sales representatives were trained to (and did) ask doctors, "Have you seen patients like HENRY in your practice?" If they had, sales representatives were trained to (and did) suggest prescribing Plavix to those individuals.

[redacted]

156 [redacted].

279. Likewise, [redacted],[157] again with no warning that [redacted] were at greater risk of non-response. Sales representatives were trained to (and did) ask doctors, "[redacted]?" If they did, sales representatives were trained to (and did) suggest prescribing Plavix to those individuals.

[redacted]

280. Sales representatives, including Evans, delivered the "Living Proof" message throughout the United States, including to the following physicians [redacted], well after the FDA had required Defendants to change the Plavix label[158] [redacted]):

- [redacted]

157 [redacted]
158 [redacted]

- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]

281. Defendants have regularly promoted Plavix to Dr. Stahl—a consultative/non-invasive cardiologist—since the drug was introduced to the market in 1998. Further, because Dr. Stahl had historically been one of the highest Plavix prescribers nationally and has a particularly high profile in the medical community, Defendants often assigned supervisory/managerial level employees to deliver their promotional pitches directly to him.

282. The following are some of the Sanofi personnel who have promoted Plavix to Dr. Stahl in the manner described in this Second Amended Complaint: (i) Andrea Schoenberg; (ii) H.J. Schroeder; (iii) Michelle L. Jenkins; (iv) Sue Sullivan; (v) Jodi Koelsch; (vi) Vanessa Galkin; (vii) Eric MacMillan; (viii) Kenneth J. Langome; (ix) Alma Zakimova; and (x) Anthony Vosilla. The following are some of the BMS personnel who have promoted Plavix to Dr. Stahl in the manner described in this Second Amended Complaint: (i) Specialty Senior Business Manager Marian Burke; (ii) Senior Territory Business Manager Craig London; and (iii) Associate Territory Business Manager Gary Pickering.

283. At no time have Defendants proactively disclosed the cytochrome P450 responsiveness problem to Dr. Stahl—even as they repeatedly told him that they were providing all the pertinent information regarding Plavix. Moreover, on numerous occasions, Defendants, through their sales representatives identified *supra*, reassured Dr. Stahl that there was no variability in efficacy for patients taking Plavix, and that, to the extent there was a problem at all, it was negligible, even though the overwhelming body of evidence demonstrated that over 30% of Plavix patients the drug was contraindicated and therefore essentially a medically unnecessary and unreasonable placebo. Thus, Dr. Stahl was left to discover the true scope of these serious, treatment altering, problems on his own through testing his patients.

284. And even then Defendants denied that the available bedside tests (to determine whether the drug was working for particular patients) were validated or clinically appropriate. Instead, they attempted to dissuade Dr. Stahl's from his concerns by telling him that the only valid testing was genetic testing, which they argued was "not clinically appropriate" due to the time and cost involved in such testing.

285. When Dr. Stahl learned of the CYP2C19 problem (through his own review of available scientific literature in approximately late 2008 during an American College of Cardiology Foundation meeting at a presentation by Dr. Valentin Fuster and in discussions then and shortly thereafter with other attendees and colleagues), he began to question Defendants' sales representatives and supervisors who promoted the drug to him about the scope and substance of the issue. Rather than tell him the truth, they falsely told him the problem was not significant, that it impacted only a small number of patients and that the data likely was skewed by extraneous factors, such as interactions with other drugs, patient failure to take Plavix as prescribed, and physician failure to prescribe Plavix for a long enough period of time. Defendants' sales representatives and supervisors identified *supra* went to great lengths to *challenge* and *obfuscate* the scientific literature in order to allay his concerns regarding variability of response and implications for the usage of Plavix. For example, they told him he should not be concerned with the non-responder issue because he treated very few Asian-Americans or African-Americans in his practice. Thus, Defendants attempted to mislead Dr. Stahl as they had other physicians into believing that their patients' failure to respond to treatment was due to their underlying disease, rather than genetic non-responsiveness to Plavix.

286. Once the Plavix label was changed in 2009 to reflect that a segment of the population was genetically predisposed to diminished (or no) responsiveness to Plavix,

Defendants' sales and marketing teams sought first to preserve their market share, and then to use the issue to expand their market share.

287. When the label for Plavix was amended in October 2009 (at the FDA's insistence) to reflect the cytochrome P450 problem, Defendants instructed their combined sales force (including Ms. Evans) to downplay its significance. Instead, they were to instructed "Expand and Protect" the Plavix market share. For example, sales representatives were instructed to discourage physicians from switching patients to Effient (prasugrel)—Lilly's competitor drug that does not depend on CYP2C19 and that had just been approved by the FDA in July 2009—by telling them:

> Importantly, there is no clinical evidence or direction in either the PLAVIX® label or my competitor's label that would recommend or even suggest that PLAVIX® patients be switched to their antiplatelet agent.

288. Of course, such a statement strains credulity, for if a patient is not responding to Plavix because of a cytochrome P450 problem, the drug may be having little more than a placebo effect on them such that switching to therapy with Effient would, in most cases, be the logical next step. Further, Defendants trained their sales force to obfuscate the issue on the basis that variability of response among individuals was "potentially attributable" to many factors other than genetic predisposition, including patient noncompliance and inadequate dosing, implicitly suggesting that physicians should address diminished response by counseling their patients and/or increasing their dosage.

289. Shortly after the Black Box Warning was inserted into the Plavix label in March 2010, Evans and Defendants' sales representatives received instruction via a Communication Plan & Responding to Customer Inquiries training about how they should respond to physician inquiries to blunt any loss of sales. Even though this was inherently deceptive, Evans and her colleagues were instructed they were to (and they did) diminish the impact of the label change, describing the

label changes as impacting only a very limited subset of patients. They were to (and they did) inform doctors misleadingly that only "poor metabolizers" "had diminished antiplatelet response":

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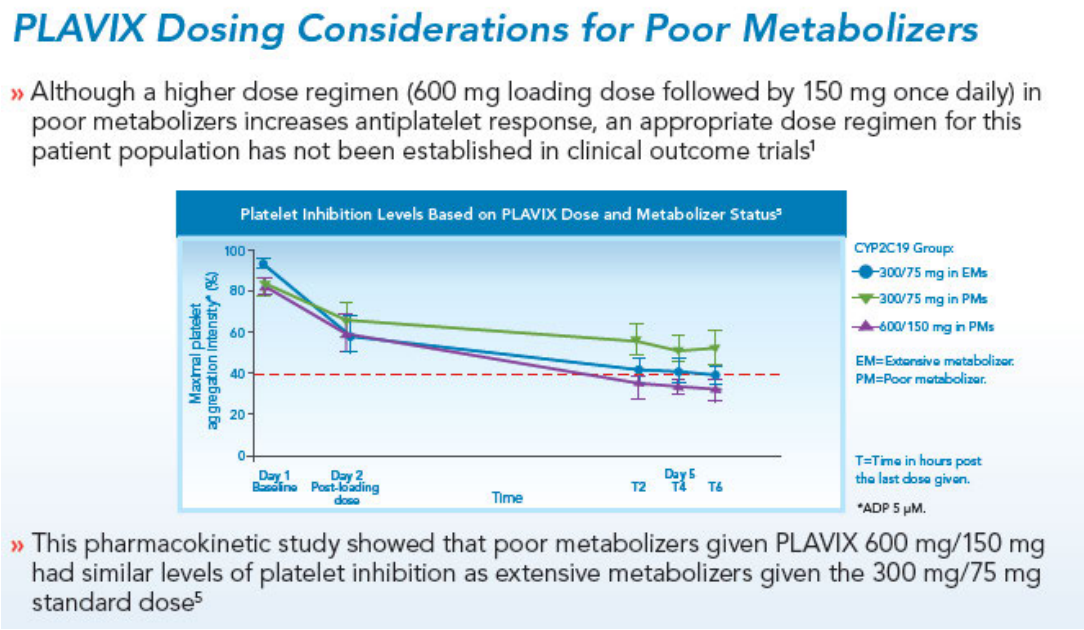
Speaker to refer to slide for presentation.

This representation also deliberately and misleadingly understated what Defendants knew were serious risks of diminished antiplatelet response for those patients with only one loss of function allele and for whom the recommended dose of Plavix would have a diminished effect.

290. Evans and her colleagues were also instructed to (and they did) detail physicians that, if they had any concerns about which of their patients were "poor metabolizers," instead of going to the expense and delay associated with platelet function testing, they could simply double the dose of Plavix (using a 600mg loading dose followed by a 150 mg once daily dose). Of course, for the double allele patients with two loss-of-function alleles (CYP2C19 *2 and *3), this strategy was ineffective since these patients very poorly metabolize Plavix, so doubling the dose for these patients had little to no effect.

291. Here is the cue card Defendants provided to their sales force to upsell physicians to prescribe double the dose for these non-responder patients:



Buried at the bottom of the cue card was a point that sales representatives were instructed they should not mention—*i.e.*, that "[a]lternative treatment strategies should be considered for patients who are determined to be CYP2C19 poor metabolizers." Not even disclosed to sales representatives or to physicians, however, was the fact that this study was based on a very small number of healthy volunteers, and that in larger studies involving PCI stent patients doubling the Plavix dose in patients with two loss of function genes was a very poor strategy to overcome resistance.

292. Cynically, Defendants responded to the FDA's required label changes by proactively encouraging physicians like Dr. Stahl to prescribe *higher* or *double doses* of Plavix to affected patients, telling them that higher doses would counteract the diminished functionality of the patient's CYP system enzymes.

293. By late 2009 and on into 2010, even though Defendants were in the declining days of the Plavix life cycle (with patent expiration due in May 2012), they would make sure their sales forces understood the "Expand & Protect" strategy. Even though the FDA had mandated that

Plavix label notify physicians of the non-responder risk, Defendants insisted still that every "[redacted]."[159]

294. The core strategy was the to "Expand & Protect" Plavix sales. Sales representatives like Evans were told that, [redacted]"

295. Even though the FDA had insisted that Defendants change the Plavix label to provide notice concerning non-responders, Defendants' message remained that all stent patients should be on Plavix: "[redacted]" helping ensure that every "[redacted]"[160]

296. Likewise, even after the Black Box Warning was inserted into the label in March 2010, Defendants' message did not change. [redacted][161]

297. At the time, Defendants' message remained that there was "[redacted]"[162] [redacted][163].

159 [redacted]
160
161
162
163 .

[redacted]

[redacted]

[redacted].

298. Defendants did tell sales representatives that, [redacted]

[redacted]

[redacted]"[164]

[redacted]

299. [redacted]

[redacted]

[164] [redacted]

[redacted][165]

300. Even though Plavix now had a Black Box Warning, Defendants nonetheless instructed their sales representatives that they should still tell physicians that "[redacted]",[166] [redacted].

301. Defendants' misguided and misleading effort to downplay and obfuscate the cytochrome P450 problem is problematic for three reasons. First, and most obviously, it put patients at risk by affirmatively misleading physicians regarding the efficacy of the drugs they prescribed for patients in need.

302. Second, it flouted the standard of care for patients who are genetically predisposed to intermediate or poor response to Plavix. Indeed, the Clinical Pharmacogenetics Implementation Consortium of the National Institutes of Health's Pharmacogenomics Research Network (an assuredly impartial body) published *peer-reviewed guidelines* for antiplatelet therapy, and those guidelines specifically and unambiguously *reject* Defendants' effort to encourage physicians to keep all antiplatelet therapy patients on Plavix. Instead, the Guidelines specifically recommended that intermediate and poor metabolizers *not* be treated with Plavix, but that they be treated with Effient or another alternative therapy instead. *See* S.A. Scott, *et al.*, *Clinical Pharmacogenetics Implementation Consortium Guidelines for Cytochrome P450-2C19 (CYP2C19) Genotype and Clopidogrel Therapy*, 90 CLIN. PHARM & THERAPEUTICS 328-32 (August 2011).

165 [redacted]
166

303. Third, dosing all patients with higher quantities of Plavix created a significant risk of *major bleeding complications* and other serious and potentially life-threatening complications.

VII. FALSE CLAIMS FOR PAYMENT ARE SUBMITTED TO GOVERNMENT PURCHASERS OF PLAVIX

A. DEFENDANTS KNOWINGLY WITHHELD INFORMATION MATERIAL TO GOVERNMENT PURCHASERS

304. Federal, state and local governments, seeking ways to lower drug costs, purchase pharmaceutical products, including Plavix, directly from drug companies like Defendants, or, through designated drug wholesalers and distributors (collectively, "Government Purchasers"). Pursuant to statutory schemes and contracts, Plavix is shipped or delivered to government-operated pharmacies, hospitals, clinics, and a wide array of other facilities for their direct use—*i.e.*, dispensing to eligible patients covered by the applicable government agency. Once delivered, Defendants, or designated wholesalers, submit invoices, or claims, to Government Purchasers for payment of Plavix each time Plavix is delivered, resulting in many thousands of separate invoices, each a false claim.

305. Federal and state laws require prescription drugs, like Plavix, shipped and sold in the United States to be safe, effective, and reliable as represented. Accordingly, as a condition to agreements to purchase Plavix, Government Purchasers required Defendants, or their wholesalers, to warrant that Plavix was FDA-approved, and fit to treat government beneficiaries. Defendants, seeking to increase Plavix sales, agreed to expressly and impliedly warrant Plavix's quality.

306. Defendants knowingly withheld information of their non-compliance with a material contractual requirement—*i.e.*, the express and implied warranties that Plavix was suitable or fit to treat Government Purchasers' beneficiaries. Defendants' material non-disclosure of Plavix's defects induced Government Purchasers to buy Plavix by preventing them from making informed decisions.

307. Claims for payment of Plavix shipments were factually false. Defendants knowingly misrepresented, or caused wholesalers to materially misrepresent Plavix's quality—*i.e.*, its fitness to treat beneficiaries' medical conditions. The true set of facts was that Plavix was not fit to treat thirty-percent of beneficiaries' medical conditions. Accordingly, purchase invoices, or claims for payment, were factually false. Simply put, when the purchase contracts require the delivery of a high-quality product, but the contractor supplies a materially less effective, lower quality product, but bills for the higher quality product, the invoice for the substandard product is "false."

308. Claims for payment of Plavix shipments were also legally false. Defendants expressly and impliedly warranted that Plavix was fit to treat beneficiaries' medical conditions. However, Defendants knowingly withheld information, prior to, and at the time agreements were executed, of their non-compliance with a material contractual requirement, the express and implied warranties that Plavix was suitable or fit to treat Government Purchasers' beneficiaries. Thus prior to and at the time of contract execution, Defendants had no intention of complying with these warranties incorporated in prime vendor contracts which were material to, and were conditions precedent to, payment by Government Purchasers.

B. FEDERAL AND STATE GOVERNMENTS PURCHASED PLAVIX

309. Federal and State Governments purchase prescription drugs, including Plavix, directly from Defendants and wholesalers, which are distributed to eligible patients in government-run medical facilities.

310. One of the earliest examples of a government purchaser is the Veteran's Administration ("VA"). Under the Veterans Health Care Act of 1992 ("VHCA") pharmaceutical manufacturers must offer reduced prices for prescription drugs to certain agencies, including, for example, the VA, the Department of Defense, and the Public Health Service, in order to participate

in Medicaid, Medicare Part B, and certain other federal funding programs. Through contractual agreements with the VA implementing the requirements of the VHCA, each manufacturer must offer its products on the VA's Federal Supply Schedule at discounted prices.

311. The VA, through its Pharmaceutical Prime Vendor Program, in fiscal year 2012, provided prescription drug coverage to about 8.8 million eligible veterans, including through its medical centers and its Consolidated Mail Outpatient Pharmacy ("CMOP"), where eligible beneficiaries can have their prescriptions filled.

312. The VA primarily uses the direct purchase approach to acquire drugs, including Plavix, directly from manufacturers for distribution through its facilities. In fiscal year 2012, VA's total prescription drug spending totaled about $4.2 billion, while its national contract purchases totaled $296.8 million.

313. The VA also purchases prescription drugs, including Plavix, for the benefit of State Veterans Homes, Indian Health Service, Immigration Health Service Corps, Department of Homeland Security, Bureau of Prisons, Howard University, Public Health Service, Commonwealth of Northern Mariana Island, Federal Health Care Centers and the Peace Corps.

314. The DOD likewise is a major purchaser of prescription drugs, including Plavix, through its Pharmaceutical Prime Vendor Program, which has been operated with coordination from the VA, or through prime vendor contracts awarded to wholesalers. DOD provides prescription drug coverage to about 9.7 million active-duty and retired military personnel, their dependents, and others, through its military treatment facilities, the TRICARE Mail Order Pharmacy ("TMOP"), retail pharmacies and other government organizations and providers located in the United States and throughout the world.

315. There are a number of prescription drug wholesalers and distributors in the United States which have done business with Defendants on behalf of Government Purchasers. These include McKesson Corporation and Cardinal Health. Each has been awarded government prime vendor contracts.

316. Wholesalers like McKesson Corporation and Cardinal Health contract with Defendants to supply prescription drugs to Government Purchasers and others. McKesson holds contracts with federal and state governments, including, for example, a pharmaceutical prime vendor contract (Contract No. V797P-1020) with the VA, which includes purchases of Plavix. The contract was awarded at the end of 2003 and was worth an estimated $2.9 billion. Cardinal Health has agreements with Group Purchasing Organizations (GPOs), which act as agents to negotiate vendor contracts on behalf of their members, which include government agencies or entities. Cardinal Health also holds contracts with federal and state governments. Businesses within its Pharmaceutical Segment, such as Cardinal Health at Home, are Medicare-certified suppliers and participants in state Medicaid programs. Wholesalers also contract with pharmacy benefit managers and other entities distributing Plavix to government beneficiaries through mail order or retail pharmacies.

317. VA and DOD beneficiaries obtain and fill their prescriptions from VA or DOD-run retail and mail pharmacies, clinics, hospitals, and medical centers. DOD allows its beneficiaries to fill prescriptions in non-DOD retail pharmacies and then reimburses those pharmacies for the cost of the drugs. In some cases, VA beneficiaries can obtain prescription drugs on a fee-for-service basis through non-VA facilities.

318. The DOD and VA are major federal purchasers of prescription drugs, including Plavix. To illustrate, in fiscal year 2012, the departments spent a combined $11.8 billion to

purchase drugs on behalf of approximately 18.5 million beneficiaries. In fiscal year 2011, the departments' expenditures, totaling about $11.3 billion, amounted to about 13 percent of all federal drug expenditures. Total DOD and VA spending includes all VA drug expenditures plus DOD's expenditures for drugs dispensed at DOD inpatient and clinic facilities as well as all outpatient prescriptions filled at the DOD's TRICARE Mail Order Pharmacy, DOD pharmacies, and non-DOD retail pharmacies.

319. The method used by DOD and VA to pay for prescription drugs on behalf of their beneficiaries is via direct contracting, with subsequent invoicing for each drug delivery. The process leading up to the negotiation of the contracts, as well as the contract terms, are very similar, if not identical. Using the direct purchase approach, the Government Purchasers contract with and purchase drugs, like Plavix, directly from manufacturers, including Defendants, or through intermediaries such as wholesalers, referred to as "prime vendors." Both Defendants and/or their designated wholesalers have been DOD or VA prime vendors.

320. For example, Defendant Bristol Myers Squib Co. has entered into prime vendor contracts (*see, e.g.*, Contract No. V797P5512N) with the VA in November of 1992, and in 2008 was awarded Contract No. V640C46153 to provide pharmaceuticals and drugs to the VA, valued at $16,597,007.

321. The prime vendor contracts include, among many other items, core terms such as delivery and payment, as well as quality assurance warranties, and are assigned a contract number. Once the master prime vendor agreement is in place, each government agency, or each of its authorized medical facilities, upon request to the prime vendor, are delivered shipments of Plavix. Subsequent to delivery, invoices are generated by the prime vendor, and submitted to the

responsible government agency, *e.g.*, VA, for payment. Record of those invoices, and receipt of payments, are in the possession of Defendants or their designated wholesalers.

322. Each invoice references the master prime vendor contract. For example, Contract No. V797P-1020 is a master prime vendor agreement awarded by the VA to wholesaler McKesson Corporation. This agreement includes purchases and deliveries of Plavix, and was signed on August 6, 2003 by McKesson Senior V.P. Paul Julian.

323. The following table set forth below provides examples of invoices submitted for payment pursuant to Contract No. V797P-1020 with wholesaler McKesson Corporation for deliveries of Plavix. Each invoice submitted constitutes a false claim[167]:

AWARD ID	COMPLETION DATE	CONTRACTING OFFICE	PLACE OF DELIVERY	VALUE OF DELIVERY*	ITEM
DJBNEL5B1 10003	10/19/04	Bureau of Prisons	NV, zip 89191	$1,300.10	Plavix 75mg
DJBNEL5B1 10007	11/12/04	Bureau of Prisons	NV, zip 89191	$2,760.05	Plavix 75mg
DJBNEL5B1 10008	11/18/04	Bureau of Prisons	NV, zip 89191	$2,674.02	Plavix 75mg
DJBNEL5B1 10012	12/16/04	Bureau of Prisons	NV, zip 89191	$2,215.58	Plavix 75mg
DJBNEL5B1 10013	12/24/04	Bureau of Prisons	NV, zip 89191	$1,736.84	Plavix 75mg
DJBNEL5B1 10017	1/21/05	Bureau of Prisons	NV, zip 89191	$2,269.80	Plavix 75mg
DJBNEL5B1 10018	1/27/05	Bureau of Prisons	NV, zip 89191	$2,777.00	Plavix 75mg
DJBNEL5B1 10018	2/02/05	Bureau of Prisons	NV, zip 89191	$2,794.88	Plavix 75mg
DJBNEL5B1 10020	2/10/05	Bureau of Prisons	NV, zip 89191	$1,140.30	Plavix 75mg
DJBNEL5B1 10024	3/11/05	Bureau of Prisons	NV, zip 89191	$588.77	Plavix 75mg
DJBNEL5B1 10026	3/31/05	Bureau of Prisons	NV, zip 89191	$1,305.81	Plavix 75mg
DJBNEL5B1 10028	4/12/05	Bureau of Prisons	NV, zip 89191	$3,007.01	Plavix 75mg
DJBNEL5B1 10034	5/27/05	Bureau of Prisons	NV, zip 89191	$725.95	Plavix 75mg
DJBNEL5B1 10035	6/01/05	Bureau of Prisons	NV, zip 89191	$1,364.69	Plavix 75mg
DJBNEL5B1 10037	6/15/05	Bureau of Prisons	NV, zip 89191	$788.12	Plavix 75mg

[167] For the 28 Bureau of Prisons entries, the "Value of Delivery" does not reflect the value of the Plavix delivered because other pharmaceutical drugs were delivered as part of the same order.

DJBNEL5B1 10038	6/23/05	Bureau of Prisons	NV, zip 89191	$1,350.68	Plavix 75mg
DJBNEL5B1 10041	7/14/05	Bureau of Prisons	NV, zip 89191	$585.32	Plavix 75mg
DJBPOL5B1 40079	7/14/05	Bureau of Prisons	Pollock, LA	$2,700.23	Plavix 75mg
DJBNEL5B1 10044	7/28/05	Bureau of Prisons	NV, zip 89191	$770.77	Plavix Tab.
DJBNEL5B1 10047	8/24/05	Bureau of Prisons	NV, zip 89191	$937.83	Plavix 75mg
DJBPOLFB1 40010	10/18/05	Bureau of Prisons	Pollock, LA	$1,938.67	Plavix Tab.
V656X63243	4/13/06	Veterans Affairs	Saint Cloud, MN	$9,492.63	Plavix 75mg
V656X63310	5/29/06	Veterans Affairs	Saint Cloud, MN	$15,214.35	Plavix 75mg
V656X63317	6/02/06	Veterans Affairs	Saint Cloud, MN	$17,181.24	Plavix 75mg
V656X63323	6/05/06	Veterans Affairs	Saint Cloud, MN	$13,313.98	Plavix 75mg
V656X63385	7/22/06	Veterans Affairs	Saint Cloud, MN	$11,564.68	Plavix 75mg
DJBPOLGB1 40080	7/29/07	Bureau of Prisons	San Francisco, CA	$2,435.44	Plavix Tab.
DJBPOLGB1 40085	8/30/07	Bureau of Prisons	San Francisco, CA	$2,432.76	Plavix Tab.
DJBPOLHB1 40014	10/25/07	Bureau of Prisons	San Francisco, CA	$3,493.23	Plavix Tab.
DJBPOLHB1 40095	6/20/08	Bureau of Prisons	San Francisco, CA	$11,045.88	Plavix Tab.
DJBPOLHB1 40100	7/02/08	Bureau of Prisons	San Francisco, CA	$7,566.15	Plavix Tab.
DJBPOLHB1 40110	7/14/08	Bureau of Prisons	San Francisco, CA	$8,696.68	Plavix Tab.
DJBPOLIB14 0041	12/12/08	Bureau of Prisons	San Francisco, CA	$5,550.50	Plavix Tab.

324. Defendants were aware of the significance and importance of Government Purchasers to Plavix sales and profits. BMS has publicly acknowledged that "state and federal governments are major purchasers and payers of BMS products. The federal government contracts with healthcare plans to provide drug benefits under Medicare Part D, reimburses for products under Medicare Part B, and participates in reimbursement to pharmacy providers under Medicaid and other programs. The government (such as the Department of Veterans Affairs or the Department of Defense) may also be a direct purchaser of BMS products. Since the government relies on BMS pricing data to determine purchase prices, reimbursement rates, and rebates for

BMS products, the Company has an obligation to accurately report BMS pricing information so that taxpayer money will be appropriately used to support these programs."

325. Recognizing the important role of governmental third party payers to Plavix's success, Defendants implemented a multi-faceted national strategy to target Government Purchasers in order to increase sales.

326. Defendants' strategies to target Government Purchasers to obtain lucrative contractual awards was a resounding success. According to a General Accounting Office report, DOD and VA spent more on Plavix 75mg than any other drug. Indeed, Plavix prescription utilization was the seventh highest for DOD, third for VA beneficiaries.

327. In addition to federal government agencies, State governments are also purchasers of Plavix. The purchasing States enter into these arrangements on behalf of their State government-funded health plans, as well as for their Medicaid beneficiaries, for dispensing to eligible patients. These States have individually or in pooled purchasing arrangements have sought to become better purchasers and benefit managers in order to achieve savings and improve care quality for the people they cover. Pooled purchasing offers the promise of cost savings and of quality improvement. In 2014, there were five operating multi-state prescription drug purchasing pools. Collectively, the States paid billions of dollars for Plavix shipments.

328. As an example, the Minnesota Multistate Contracting Alliance for Pharmacy (MMCAP or "State") is a voluntary group purchasing organization for states and local government facilities nationwide and is managed by the Materials Management Division of the State of Minnesota's Department of Administration. It primarily contracts directly with pharmaceutical manufacturers/suppliers for their products and uses pharmaceutical wholesalers to deliver the products to its member facilities. Defendants are MMCAP contracted suppliers.

329. MMCAP Participating Facilities are located across the nation and purchase over $1 billion of pharmaceuticals and other medical related supplies per year. Participation in MMCAP is available to government facilities with authority to contract with the State of Minnesota. MMCAP Participating Facilities are state agencies and political subdivisions that primarily fall under the following classes of trade: correctional facilities, psychiatric treatment facilities, student health services, public health services, non-federal veterans' nursing homes and public hospitals.

330. MMCAP's membership includes thousands of participating governmental health care facilities, located in all 50 states, including Alabama, Alaska, Arizona, Arkansas, California, Colorado, Connecticut, Delaware, Florida, Georgia, Hawaii, Idaho, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maine, Maryland, Michigan, Minnesota, Mississippi, Missouri, Montana, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, South Dakota, Tennessee, Texas, Utah, Vermont, Virginia, Washington, West Virginia, Wisconsin and Wyoming.

331. MMCAP enters into purchase agreements, including prime vendor agreements, which require, as a condition of payment, compliance with contract, as well as federal, state and local laws, as applicable to each member state. Like the VA and DOD, the individual state members place Plavix orders referencing the MMCAP master vendor contract, and are separately invoiced, each invoice constituting a false claim.

C. GOVERNMENT PURCHASERS REQUIRE PRIME VENDORS TO WARRANT THAT THEIR DRUG PRODUCTS ARE EFFECTIVE FOR GOVERNMENT PURCHASER BENEFICIARIES

332. Government Purchasers' primary purpose in awarding lucrative prime vendor contracts is to (1) ensure a reliable source of effective and safe prescription drugs for all their beneficiaries, and (2) reduce costs.

333. Prior to awarding prime vendor contracts, Government Purchasers engage in a process involving requests for proposals, responses to those requests, negotiation, and finally execution of a written prime vendor agreement. As a condition of awarding the contract, prime vendors like Defendants must agree to certain key assurances and/or warranties, key among those are assurances as to the quality of their drug products.

334. Government Purchasers strive to ensure the safety and efficacy of drug products, as they are taken daily by millions of their beneficiaries, through a combination of federal approvals, inspections, enforcement, and self-regulation by drug manufacturers. As the FDA's Deputy Associate General Counsel, Eric M. Blumberg, Esq., wrote, drug manufacturers "occupy a virtual fiduciary relationship to the public. . . . FDA shares this trustee relationship to the consumer with industry leaders, but the initial and ultimate responsibility remains with those leaders."

335. Federal, state and local governments justifiably rely on drug manufacturers like Defendants to provide assurances that Plavix is a safe and effective drug product, suitable for all their beneficiaries' use. These assurances and warranties are included in prime vendor contracts, and go the essence of the bargain between Defendants and Government Purchasers.

336. Defendants knew that Government Purchasers of Plavix relied on their assurances, representations and/or warranties as to Plavix's efficacy and safety when making prime vendor awards, and then paying invoices valued at billions of dollars for Plavix.

D. DEFENDANTS MATERIALLY MISREPRESENT PLAVIX'S FITNESS AND SUITABILITY TO GOVERNMENT PURCHASERS

337. Defendants knowingly withheld information of their non-compliance with a material contractual requirement, the express and implied warranties that Plavix was suitable or fit to treat Government Purchasers' beneficiaries. Defendants' material non-disclosure of Plavix's

quality induced Government Purchasers to buy and pay for Plavix by preventing Government Purchasers from making informed decisions to buy Plavix.

338. Defendants were not truthful during the prime vendor award process, at the time of the execution of the prime vendor agreements, or when invoices or claims for payment were submitted to Government Purchasers of Plavix. These misrepresentations and omissions, as well as related false certifications of compliance with applicable core laws and warranties, were material to the Government Purchasers' decisions to buy and pay for Plavix.

339. Defendants took advantage of the trust placed in them by Government Purchasers by knowingly concealing the truth about Plavix's efficacy and safety—*i.e.*, that Plavix is ineffective, unsafe, even potentially deadly, for over 30% of government purchaser beneficiaries for whom the drug was contraindicated and therefore essentially a medically unnecessary and unreasonable placebo.

340. Having been deceived by Defendants' deception, Governmental Purchasers purchased Plavix for distribution to patients, an unknown number, estimated to be over 30%, for whom Plavix was ineffective and unsafe.

341. Defendants also violated the FCA by falsely certifying that Plavix was free of defects, and like other products purchased by the Government Purchasers, was suitable for its intended use—*i.e.*, effective for all patient populations. The VA agreements contain the following representation which was made by Defendants as to Plavix:

> Warranty. The Contractor warrants and implies that the items delivered hereunder are merchantable and fit for use for the particular purpose described in this contract.

342. Defendants entered into prime vendor agreements containing this or similar warranties, despite having knowledge that Plavix was not fit for use by all patient populations.

343. These warranties, assurances or certifications as to fitness for use are material to the government decisions to pay for Plavix. For example, the VA Pharmaceutical Prime Vendor Contract VA797P-12-D-0001 directly addresses circumstances involving defective products:

> The Government may require repair or replacement of nonconforming supplies or re-performance of nonconforming services at no increase in contract price. The Government must exercise its post-acceptance rights (1) Within a reasonable time after the defect was discovered or should have been discovered; and (2) Before any substantial change occurs the condition of the item, unless the change is due to the defect in the item.

344. Defendants are also required to comply with applicable laws: "The Contractor shall comply with all applicable Federal, State and local laws, executive orders, rules and regulations applicable to its performance under this contract."

345. The inclusion of provisions in the Government Purchasers' contracts demonstrates the critical importance of non-defective prescription drug products to be distributed to beneficiaries. For example, the VA prime vendor contract includes a section on drug recalls, which requires expeditious notifications broadcast to a wide number of agencies. In addition, the drug manufacturer must issue replacement product or credit for any product recalled.

346. Recalls occur when drugs have been found to be adulterated, ineffective, or otherwise not fit for their intended use. Plavix has not been the subject of a recall; however, the VA contract language cited above illustrates the critical importance to the VA to ensure the quality of the prescription drugs it purchases.

347. Defendants knew that the Government Purchasers relied on Defendants' representations and certifications when entering into purchase agreements, and that they had bargained and paid for an assurance of quality and fitness for use that it did not receive from Defendants.

348. At the time Defendants expressly certified that the prescription drugs, including Plavix, were free of defects, and suitable for use in all patient populations, Defendants knew that those certifications were false, and knew that the Government Purchasers relied on Defendants' certifications when awarding prescription drug purchase contracts.

349. At the time Defendants expressly certified that the prescription drugs provided to the Government Purchasers were free of defects, and suitable for use in all patient populations, Defendants knew that those certifications were false, Defendants' subsequent invoices submitted or caused to be submitted to the Government Purchasers were impliedly false.

E. DEFENDANTS' KNOWINGLY WITHHELD INFORMATION OF THEIR NON-COMPLIANCE WITH MATERIAL CONTRACT REQUIREMENTS PRIOR TO AND SUBSEQUENT TO THE AWARDS

350. Defendants knowingly withheld information of their non-compliance with a material contractual requirement, the express and implied warranties that Plavix was suitable or fit to treat Government Purchasers' beneficiaries. Defendants' material non-disclosure of Plavix's quality induced Government Purchasers to buy and pay for Plavix by preventing Government Purchasers from making informed decisions to buy Plavix.

351. As alleged in this Second Amended Complaint, Defendants falsely certified compliance with statutory, regulatory, and contractual requirements which were material to the Government Purchasers' payment decisions, and conspired to submit false claims to the government, all in order to sell more Plavix.

352. As a result of Defendants' material misrepresentations (*i.e.*, that Plavix was free of defects, and suitable for use in all patient populations) when Defendants knew that those representations were false, being material half-truths, Defendants made or caused to be made to Government Purchasers false claims for payment for Plavix. These misrepresentations, or half-truths, were not minor or insubstantial, as they go to the heart of Defendants' role in selling

prescription drugs to Government Purchasers to be distributed to their beneficiaries. These misrepresentations were sufficiently important to influence the Government Purchasers.

353. Defendants' misrepresentations, and related false certifications, caused Government Purchasers to pay for an assurance of quality and fitness for Plavix's use that it did not have, financially damaging Government Purchasers.

VIII. DEFENDANTS VIOLATED THEIR CORPORATE INTEGRITY AGREEMENTS BY INTENTIONALLY FALSIFYING OR CONCEALING THEIR ILLEGAL CONDUCT IN REPORTS SUBMITTED TO THE GOVERNMENT IN ORDER TO OBTAIN ILLEGAL REIMBURSEMENT

354. In order to execute its unlawful conduct, Defendants needed to conceal their illegal conduct from Government oversight, particularly in light of the fact that each was operating under its own Corporate Integrity Agreement ("CIA" or "Agreement").

355. Accordingly, Defendants engaged in a deliberate plan to knowingly submit false reports to the OIG—as required per the terms of each CIA—that either materially misrepresented the facts concerning their illegal conduct or concealed such conduct altogether.

356. Defendants, through their Compliance Departments, (1) falsely certified in their periodic reports to the Government that they had fully complied with their CIA obligations; (2) ignored data obtained via third-party audits to minimize the true extent of Defendants' misleading promotional activities promotion; and (3) concealed from the Government reportable events that were brought to Defendants' attention by these audits.

357. As such, Defendants knowingly made, used, or caused to be made or used, false records or statements that were material to an obligation to pay or transmit money or property to the Government, or knowingly concealed or knowingly and improperly avoided or decreased an obligation to pay or transmit money or property to the Government.

A. THE CORPORATE INTEGRITY AGREEMENTS ESTABLISHED DEFENDANTS' MONITORING AND REPORTING OBLIGATIONS

358. As discussed previously, Sanofi and BMS are each under separate CIAs as part of their settlements with the Federal Government arising out of allegations that they each engaged in illegal pricing and promotion.

359. With regard to Sanofi, the Federal Government alleged that the company had engaged in a scheme to set and maintain fraudulent and inflated prices for Anzemet®, knowing that Government Programs established reimbursement rates based on those prices. In settlement of those allegations in 2007, Sanofi was required to enter into a five-year CIA that expressly incorporated measures aimed at prohibiting the Company from engaging in any further off-label promotion or fraudulent pricing schemes. *See* Sanofi CIA, *available at* https://oig.hhs.gov/fraud/cia/agreements/sanofi%20aventis%20CIA.pdf.

360. Also, in 2007, BMS and its wholly owned subsidiary, Apothecon, Inc., agreed to pay over $515 million to resolve a broad array of civil allegations involving their drug marketing and pricing practices. As part of the settlement, BMS entered into a five-year CIA that, among other things, required the company to report accurate average sales prices and average manufacturer prices for its drugs covered by Medicare and other federal health care programs. *See* BMS CIA, *available at* http://www.pharmacomplianceforum.org/docs/resources/BristolMyersSquibbCIA.pdf.

361. Each CIA is an express contract between Defendants, the U.S. Department of Health and Human Services and the United States Government.

362. All of Defendants' employees were aware of the CIAs, as the CIAs required a written Code of Conduct be distributed to all Covered Persons, and each Covered Person was required to certify, in writing, that he or she had received, read, understood, and would abide by

this Code of Conduct. *See* Sanofi CIA at 5, Section III.B.1 (defining "Code of Conduct"); BMS CIA at 7, Section III.B.1 (same).

363. Each Code of Conduct was to specify that all Covered Persons were expected to comply with the requirements of the CIA. *Id*. Per the CIAs, a "Covered Person" included Defendants' officers, directors, and United States-based employees. *See* Sanofi CIA at 2, Section II.C.1.a; BMS CIA at 3, Section II.C.1.a.

364. BMS's Code of Conduct contains its commitment "to market, sell, promote, research, develop, provide information about, and advertise its products in accordance with Federal health care program and FDA requirements." *See* BMS CIA at 7, Section III.B.1.a. Similarly, Sanofi made its own commitment "to promote, sell, and market Government Reimbursed Products . . . in accordance with Federal health care program requirements." *See* Sanofi CIA at 5, Section III.B.1.a.

365. The CIAs also contained an express contractual agreement that all Defendants' employees "shall be expected to report to the Chief Compliance Officer, or other individual designated by [Defendants], suspected violations of any Federal health care program and FDA requirements or of [Defendants'] own Policies and Procedures." *See* Sanofi CIA at A at 5, Section III.B.1.c; BMS CIA at 8, Section III.B.1.c. The CIAs further required Defendants to notify the Government of any "reportable events," defined to include any "matter that a reasonable person would consider a probable violation of criminal, civil, or administrative laws applicable to any Federal health care program, and/or applicable to any FDA requirements relating to the promotion of Cephalon products for which penalties or exclusion may be authorized." *See* Sanofi CIA at 16, Section III.H.1; BMS CIA at 23-24, Section III.H.1. Defendants intentionally ignored that requirement.

366. Importantly, the CIAs established a duty and obligation to pay the Government money, in the form of stipulated penalties, which arise from Defendants' contractually-binding requirement to report instances of fraudulent conduct.

367. Specifically, each CIA contains a section entitled "Breach and Default Provisions," which provides "Stipulated Penalties" as a contractual remedy for any failure by Defendants to comply with their obligations under their respective CIAs. *See* Sanofi CIA at 28-33, Section X; BMS CIA at 42-48. These stipulated penalties include, *inter alia*:

- "A Stipulated Penalty of $2,500 (which shall begin to accrue on the day after the date the obligation became due) for each day [Defendants] fail[] to establish, implement, or accomplish any of the following obligations," including, but not limited to, "a Disclosure Program" as required by Section III.E. *See* Sanofi CIA at 28, Section X.A.1.f.; BMS CIA at 42-43, Section X.A.1.f.
- "A Stipulated Penalty of $5,000 for each false certification submitted by or on behalf of [Defendants] as part of [their] Implementation Report, Annual Report, additional documentation to a report (as requested by the OIG), or otherwise required by this CIA." *See* Sanofi CIA at 29, Section X.A.6.; BMS CIA at 44, Section X.A.6.; and
- "A Stipulated Penalty of $1,000 for each day [Defendants] fail[] to comply fully and adequately with any obligation of this CIA." *See* Sanofi CIA at 29, Section X.A.7.; BMS CIA at 44, Section X.A.7

B. INTERNAL AUDITS REVEALED DEFENDANTS' MISLEADING PROMOTION OF PLAVIX

368. As discussed *supra*, Defendants implemented an "Expand and Protect" campaign by which they promoted Plavix's purported safety and efficacy in *all* patients, although

[redacted] had shown otherwise. Evans was instructed to deliver the "Expand and Protect" message without informing prescribers what Defendants' already knew—*i.e.*, that Plavix did not work at all for a certain subset of patients and that there was a risk that the drug would not work for another subset, which, taken together, accounted for over 30% of the entire patient population.

369. And a review of the annual audit reports that Defendants were required to perform as part of their obligations under their CIAs confirms Evans's experience and observations.

370. Specifically, as part of each of their CIAs, Defendants agreed to perform internal audits to determine whether their promotional activities going forward were compliant with Federal law, and thereafter to report any further compliance issues to the Government.

371. From at least 2008 through 2012, Defendants conducted numerous internal audits of its sales force's activities to determine what, if any, compliance issues existed. As part of the audits, which were conducted by independent third parties contracted by Defendants, various healthcare providers were contacted and asked about their latest discussions with Plavix sales representatives.

372. The results of the audits revealed that Defendants' sales representatives [redacted]. The audits capture the precise messaging Defendants' sales representatives were using to promote Plavix to physicians. The following verbatim responses, reported by the audited physicians from [redacted] through [redacted], provide a sampling of how Defendants' unlawful promotional scheme was carried out by its sales representatives:

- "[redacted]"[168]

168 [redacted]

- "[redacted]"[169]
- "[redacted]"[170]
- "[redacted]"[171].
- "[redacted]"[172]
- "[redacted]"[173]

The Corporate Integrity Agreement audit results confirm not only the unlawful promotional message Evans had been instructed to deliver, but also that this message successfully reached its targeted physician audience through Defendants' sales force.

C. DEFENDANTS KNOWINGLY FAILED TO COMPLETELY AND TRUTHFULLY REPORT ALL "REPORTABLE EVENTS" IN COMPLIANCE WITH THEIR CIAS

373. Based on the audit results, Defendants' Compliance Departments were made fully aware that their sales forces were carrying out their instructions to conceal issues related to VOR. Yet, Sanofi and BMS elected to keep this issue not only from the OIG, but from their sales forces as well. Evans was never made aware that the VOR issue had been flagged as part of the audit process. Rather, Evans and her colleagues were informed of other issues related to the unlawful promotion of Plavix (and other products), but were always kept in the dark as to the VOR issue.

374. A review of the "Reportable Events" that Defendants were required to disclose to OIG as part of their obligations under the CIA confirms that Defendants intended to keep hidden the issues related to VOR. Defendants categorically refused to report to the OIG these untrue and

169 [redacted]
170
171
172
173

misleading safety and efficacy claims. When Defendants intentionally concealed this unlawful promotion, they violated the terms of their CIAs.

375. The CIAs notwithstanding, Defendants continued their illegal activities at a considerable cost to Government Programs and taxpayers. On that basis, Defendants knowingly failed to completely and truthfully certify their compliance with their respective CIAs, and they failed to completely and truthfully report all "reportable events" in compliance with the CIA. Thus, Defendants knowingly, deliberately and without just cause presented or caused to be presented false certifications or claims in violation of 31 U.S.C. § 3729(a)(1)(G).

376. As a result of Defendants' unlawful conduct, the United States has been damaged, and continues to be damaged, by Government Program payments for illegally promoted Plavix prescriptions.

IX. DEFENDANTS CAUSED PHARMACIES AND OTHER HEALTH CARE PROVIDERS TO FALSLEY CERTIFY COMPLIANCE WITH LAWS MATERIAL TO GOVERNMENT PROGRAMS' DECISIONS TO REIMBURSE OR PAY FOR PLAVIX

377. As a prerequisite for participation in, and condition-precedent to submitting claims and receiving payment from Government Programs, healthcare providers, such as pharmacies and physicians, are required to comply with applicable laws, rules and regulations governing the respective Government Programs. Non-compliance with laws rules and regulations which are material to Government Programs' reimbursement decisions render pharmacy or medical claims ineligible for payment.

378. Laws, rules and regulations which are material include those which are central to program integrity and patients' health and safety. Government Programs only cover drugs that are safe and effective (*see, e.g.*, 30.1.5 Medicare Prescription Drug Benefit Manual, Part D Drugs and Formulary Requirements), and, when FDA-approved drugs are dispensed or distributed to

government beneficiaries, that medically appropriate drugs end up in the medicine cabinet of patients in a condition that renders the drugs fit for their intended use. For example, when FDA-approved drugs are later deemed to be materially misbranded and/or adulterated, and thus ineffective or unsafe, those drugs are no longer fit for their intended use, rendering them ineligible for reimbursement by Government Programs. The same would be true for a drug like Plavix which is contraindicated and therefore essentially a medically unnecessary and unreasonable and unreasonable placebo for over 30% of the treatment population.

379. As alleged in this Second Amended Complaint, the intended, natural and foreseeable consequence of Defendants' scheme was the submission of false Plavix claims to Government Programs for a substandard drug product. The false claims are also for a misbranded drug as a result of Defendants' perpetuation of the half-truth that Plavix is effective for all patient populations, and by failing to provide prescribers adequate instructions for Plavix's safe and effective use. Thus, when pharmacies submit claims for Plavix, Defendants have caused the submission of false claims to Government Programs.

380. Pharmacy claims submitted for Plavix which involve express or implied false certifications as to safety and efficacy are thus material to Government Programs' decision to reimburse or cover Plavix claims. Safety and efficacy concerns are materially heightened when a drug like Plavix is touted by its maker as, and thus intended to be, a life-saving or life-extending drug.

381. As alleged in this Second Amended Complaint, Defendants caused pharmacies to falsely certify their compliance with core requirements that prescription drug claims to be paid from the government fisc only include drugs that do not present a risk of injury or gross deception,

and are not for dangerous or defective products that predictably could cause serious health problems or death.

382. Claims for Plavix are typically submitted electronically, whereby the pharmacies affix their unique Medicaid provider identification numbers, which serve as electronic stamps indicating that (as Medicaid providers) they are in compliance with all program requirements and all applicable federal and state laws. The electronic claim also includes the dispensed drug's National Drug Code ("NDC") number identifying the manufacturer, formulation, strength and quantity. Since NDC numbers are only issued for drugs meeting all FD&CA requirements for entry into interstate commerce, this number on the claim form represents that the drug's formulation is FDA-approved and that the product being dispensed is not materially adulterated and/or misbranded. The pharmacies are then reimbursed on a monthly basis by the *Qui Tam* States for Plavix claims. In the present case, the pharmacies' submissions included claims for materially defective and/or misbranded Plavix. As such, Defendants' caused the pharmacies to unwittingly make false certifications concerning facts that were material to Medicaid reimbursement.

383. State Medicaid provider agreements include requirements that pharmacies will comply with laws, rules, and regulations governing the Medicaid program. Although the Medicaid Provider Application varies from state to state, the provider typically affirms and undertakes compliance with all applicable state and Federal laws.

384. In the case of Medicare, participating pharmacies dispensed Plavix to beneficiaries throughout the United States. Pharmacies have contractual agreements with Medicare Part D contractors, whereby the pharmacies have agreed to provide pharmaceuticals to Medicare-eligible patients, and the Part D contractors would reimburse the pharmacies their costs plus a fixed dispensing fee meant to provide the pharmacies with a profit for providing pharmaceutical

products to Medicare patients. Pharmacies are required as a condition of payment to comply with certain laws, and are not legally permitted to dispense and submit claims for materially defective, misbranded or adulterated drugs. Pharmacies are required to abide by and certify compliance with all laws, rules, and regulations governing the Medicare program. *See, e.g.*, 42 C.F.R. § 423.505(k)(3). Defendants' scheme caused pharmacies to falsely certify their compliance with laws prohibiting dispensing of Plavix to Medicare beneficiaries.

385. In the standard Medicare Provider Agreement, the provider expressly agrees as a condition of payment to comply as follows:

> I agree to abide by the Medicare laws, regulations and program instructions that apply to [me]. The Medicare laws, regulations, and program instructions are available through the [Medicare] contractor. I understand that payment of a claim by Medicare is conditioned upon the claim and the underlying transaction complying with such laws, regulations, and program instructions (including, but not limited to the Federal Anti-Kickback statute and the Stark law), and on the [provider's] compliance with all applicable conditions of participation in Medicare.

See Form CMS-855A (for institutional providers); Form CMS-855I (for physicians and non-physician practitioners; Form 855-S (for Durable Medical Equipment, Prosthetics, Orthotics and Supplies (DMEPOS) Suppliers).

386. Even where the Provider Application and Provider Agreement are construed as an undertaking of future compliance rather than an ongoing express certification of compliance, that undertaking is sufficient to render the ensuing claims for payment an implied certification of compliance with the stated conditions of payment.

387. A common standardized health insurance claim form, Form-1500, is used for multiple Government Programs such as Medicare, TriCare, CHAMPUS, VA, Medicaid and the FEHBP. Form-1500 requires the medical provider to expressly affirm that "any false claims, statements, or documents, or concealment of a material fact, may be prosecuted under applicable

Federal or State laws." Form-1500 also requires providers to certify that the claim for reimbursement represents the provision of health care that is "medically indicated and necessary to the health" of patients. Therefore, each time providers unwittingly prescribed Plavix to over 30% of patients for whom it had no pharmacodynamic effect, they were prescribing a contraindicated drug that was essentially a medically unnecessary placebo.

388. Under the Medicare Part D program, the "claim" is the electronic Prescription Event Data ("PDE") submitted by the pharmacies to the Pharmacy Benefit Manager ("PBM") administering claims on behalf of a particular Part D Provider who has contracted with CMS. As part of the PDE, the pharmacies affix their unique Medicare provider identification numbers, which serve as electronic stamps indicating that (as Medicare providers) they are in compliance with all program requirements and all applicable federal and state laws. The electronic claim also includes the dispensed drug's National Drug Code ("NDC") number identifying the manufacturer, formulation, strength and quantity. Since NDC numbers are only issued for drugs meeting all FD&CA requirements for entry into interstate commerce, this number on the claim form represents that the drug's formulation is FDA-approved and that the product being dispensed is not materially adulterated and/or misbranded. The pharmacies are then reimbursed on a monthly basis by the Part D Provider, through the administering PBM, for Plavix claims. In the present case, the pharmacies' submissions included claims for materially defective and/or misbranded Plavix prescriptions. As such, Defendants' caused the pharmacies to unwittingly make false certifications concerning facts that were material to Medicare reimbursement.

389. As alleged in this Second Amended Complaint, Defendants' fraudulent scheme caused medical and pharmacy providers to falsely certify their compliance with laws and Government Program requirements when submitting claims for defective Plavix.

Count I

(Violation of False Claims Act, 31 U.S.C. § 3729(a)(1)(A)[174] and State Analogues)

390. Relator re-alleges and incorporates by reference all prior paragraphs.

391. Defendants knowingly presented and caused to be presented, and may still be presenting or causing to be presented, to the Government false or fraudulent claims for payment, in violation of 31 U.S.C. § 3729(a)(1)(A) and the State analogues thereto.[175]

392. As a result of Defendants' actions, as set forth above, the United States of America has been, and may continue to be, severely damaged.

Count II

(Violation of False Claims Act, 31 U.S.C. § 3729(a)(1)(B)[176] and State Analogues)

393. Relator re-alleges and incorporates by reference all prior paragraphs.

394. As a result of Defendants' actions, Defendants knowingly made, used, or caused to be made or used, and may still be making, using, or causing to be made or used, false or fraudulent claims, records or statements material to the payment of false or fraudulent claims, thereby causing false or fraudulent claims for payment to actually be paid or approved, in violation of 31 U.S.C. § 3729(a)(2) and 31 U.S.C. § 3729(a)(1)(B), and the State analogues thereto.[177]

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[174]To the extent wrongdoing occurred prior to May 20, 2009, this Complaint should be deemed to include violations of the Federal False Claims Act prior to its recent amendments, *e.g.*, 31 U.S.C. § 3729(a)(1).

[175]Cal. Gov't Code § 12651(a)(1); Col. Rev. Stat. § 25.5-4-305(a); Conn. Gen. Stat. § 4-275(a)(1); Del. Code Ann. Tit. 6, § 1201(a)(1); D.C. Code § 2-308.14(a)(1); Fla. Stat. § 68.082(2)(a); Ga. Code Ann. § 49-4-168(a)(1); 740 Ill. Comp. Stat. 175/3(a)(1)(A); Ind. Code § 5-11-5.5-2(b)(1); Iowa Code § 685.2(1)(a); La. Rev. Stat. Ann. § 46:438.3(A); Mass. Gen. Laws ch. 12 § 5B(a)(1); Mich. Comp. Laws § 400.607(1); Minn. Stat. § 15C.02(a)(1); Mont. Code Ann. § 17-8-403(1)(a); Nev. Rev. Stat. § 357.040(1)(a); N.J. Stat. Ann. § 2A:32C-3(a); N.Y. State Fin. Law § 189(1)(a); N.C. Gen. Stat. § 1-607(a)(1); Okla. Stat. tit. 63, § 5053.1(B)(1); R.I. Gen. Laws § 9-1.1-3(a)(1); Tenn. Code Ann. § 71-5-182(a)(1)(A); Tenn. Code Ann. § 4-18-103(a)(1); Tex. Hum. Res. Code Ann. § 36.002(1); Va. Code Ann. § 8.01-216.3(A)(1); Wash Rev. Code § 74.66.020(1)(a); Wis. Stat. § 20.931(2)(a).

[176] To the extent wrongdoing occurred prior to May 20, 2009, this Complaint should be deemed to include violations of the Federal False Claims Act prior to its recent amendments, *e.g.*, 31 U.S.C. § 3729(a)(2).

[177] Cal. Gov't Code § 12651(a)(2); Col. Rev. Stat. § 25.5-4-305(b); Conn. Gen. Stat. § 4-275(a)(2); Del. Code Ann. Tit. 6, § 1201(a)(2); D.C. Code § 2-308.14(a)(2); Fla. Stat. § 68.082(2)(b); Ga. Code Ann. § 49-4-168(a)(2); 740 Ill. Comp. Stat. 175/3(a)(1)(B); Ind. Code § 5-11-5.5-2(b)(2); Iowa Code § 685.2(1)(b);

395. The United States of America, unaware of the falsity of the claims and/or statements made by Defendants, and in reliance on the accuracy of these claims and/or statements, paid and may still be paying or reimbursing for Plavix prescribed to patients enrolled in Government Programs.

396. As a result of Defendants' actions, as set forth above, the United States of America has been, and may continue to be, severely damaged.

Count III
(Violation of Federal False Claims Act, 31 U.S.C. § 3729(a)(1)(G) and State Analogues)

397. Relator re-alleges and incorporates by reference all prior paragraphs.

398. As detailed above, Defendants knowingly made, used, and/or caused to be made or used, false records or statements material to an obligation to pay or transmit money or property to the Government, and/or knowingly concealed or knowingly and improperly avoided or decreased an obligation to pay or transmit money or property to the Government pursuant to 31 U.S.C. § 3729(a)(1)(G) and the State analogues thereto.[178]

399. As a result of Defendants' actions as set forth above, the United States of America has been, and may continue to be, severely damaged.

La. Rev. Stat. Ann. § 46:438.3(B); Mass. Gen. Laws ch. 12 § 5B(a)(2); Mich. Comp. Laws § 400.603; Minn. Stat. § 15C.02(a)(2); Mont. Code Ann. § 17-8-403(1)(b); Nev. Rev. Stat. § 357.040(1)(a); N.J. Stat. Ann. § 2A:32C-3(b); N.Y. State Fin. Law § 189(1)(b); N.C. Gen. Stat. § 1-607(a)(2); Okla. Stat. tit. 63, § 5053.1(B)(2); R.I. Gen. Laws § 9-1.1-3(a)(2); Tenn. Code Ann. § 71-5-182(a)(1)(B); Tenn. Code Ann. § 4-18-103(a)(2); Va. Code Ann. § 8.01-216.3(A)(2); Wash Rev. Code § 74.66.020(1)(b); Wis. Stat. § 20.931(2)(b).

[178] Cal. Gov't Code § 12651(a)(7); Col. Rev. Stat. § 25.5-4-305(f); Conn. Gen. Stat. § 4-275(a)(7); Del. Code Ann. Tit. 6, § 1201(a)(7); D.C. Code § 2-308.14(a)(7); Fla. Stat. § 68.082(2)(g); Ga. Code Ann. § 49-4-168(a)(7); 740 Ill. Comp. Stat. 175/3(a)(1)(G); Ind. Code § 5-11-5.5-2(b)(6); Iowa Code § 685.2(1)(g); La. Rev. Stat. Ann. § 46:438.3(C); Mass. Gen. Laws ch. 12 § 5B(a)(9); Mich. Comp. Laws § 400.607(3); Minn. Stat. § 15C.02(a)(7); Mont. Code Ann. § 17-8-403(1)(g); Nev. Rev. Stat. § 357.040(1)(g); N.J. Stat. Ann. § 2A:32C-3(g); N.Y. State Fin. Law § 189(1)(g); N.C. Gen. Stat. § 1-607(a)(7); Okla. Stat. tit. 63, § 5053.1(B)(7); R.I. Gen. Laws § 9-1.1-3(a)(7); Tenn. Code Ann. § 71-5-182(a)(1)(D) and/or Tenn. Code Ann. § 4-18-103(a)(7); Va. Code Ann. § 8.01-216.3(A)(7); Wash Rev. Code § 74.66.020(1)(g); Wis. Stat. § 20.931(2)(g).

Count IV
(Violation of False Claims Act, 31 U.S.C. § 3729(a)(1)(C)[179] and State Analogues)

400. Relator re-alleges and incorporates by reference all prior paragraphs.

401. As detailed above, Defendants knowingly conspired, and may still be conspiring, with the various health care professionals identified and described herein to commit acts in violation of 31 U.S.C. §§ 3729(a)(1)(A) and (a)(1)(B), all in violation of 31 U.S.C. § 3729(a)(1)(C) and the State analogues thereto.[180] Defendants and these health care professionals committed overt acts in furtherance of the conspiracy as described above.

402. As a result of Defendants' actions, as set forth above, the United States of America has been, and may continue to be, severely damaged.

Count V
(Violation of False Claims Act, 31 U.S.C. § 3729(a)(1)(C)[181] and State Analogues)

403. Relator re-alleges and incorporates by reference all prior paragraphs.

404. As detailed above, Sanofi knowingly conspired with BMS, in part through operation of the BMS/Sanofi Partnership but not only through the BMS/Sanofi Partnership, to commit acts in violation of 31 U.S.C. § 3729(a)(1)(A)-(a)(1)(B) with respect to the promotion and sale of Plavix, all in violation of 31 U.S.C. § 3729(a)(1)(C) and the State analogues thereto. [182]

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[179] To the extent wrongdoing occurred prior to May 20, 2009, this Complaint should be deemed to include violations of the Federal False Claims Act prior to its recent amendments, *e.g.*, 31 U.S.C. § 3729(a)(3).

[180] Cal. Gov't Code § 12651(a)(c); Col. Rev. Stat. § 25.5-4-305(g); Conn. Gen. Stat. § 4-275(a)(c); Del. Code Ann. Tit. 6, § 1201(a)(3); D.C. Code § 2-308.14(a)(3); Fla. Stat. § 68.082(2)(c); Ga. Code Ann. § 49-4-168(a)(3); 740 Ill. Comp. Stat. 175/3(a)(1)(C); Ind. Code § 5-11-5.5-2(b)(7); Iowa Code § 685.2(1)(c); La. Rev. Stat. Ann. § 46:438.3(D); Mass. Gen. Laws ch. 12 § 5B(a)(3); Mich. Comp. Laws § 400.606(1); Minn. Stat. § 15C.02(a)(3); Mont. Code Ann. § 17-8-403(1)(c); Nev. Rev. Stat. § 357.040(1)(c); N.J. Stat. Ann. § 2A:32C-3(c); N.Y. State Fin. Law § 189(1)(c); N.C. Gen. Stat. § 1-607(a)(3); Okla. Stat. tit. 63, § 5053.1(B)(3); R.I. Gen. Laws § 9-1.1-3(a)(3); Tenn. Code Ann. § 71-5-182(a)(1)(C) and/or Tenn. Code Ann. § 4-18-103(a)(3); Va. Code Ann. § 8.01-216.3(A)(3); Wash. Rev. Code § 74.66.020(1)(c); Wis. Stat. § 20.931(2)(c).

[181] To the extent wrongdoing occurred prior to May 20, 2009, this Complaint should be deemed to include violations of the Federal False Claims Act prior to its recent amendments, *e.g.*, 31 U.S.C. § 3729(a)(3).

[182] Cal. Gov't Code § 12651(a)(c); Col. Rev. Stat. § 25.5-4-305(g); Conn. Gen. Stat. § 4-275(a)(c); Del. Code Ann. Tit. 6, § 1201(a)(3); D.C. Code § 2-308.14(a)(3); Fla. Stat. § 68.082(2)(c); Ga. Code Ann. § 49-

Sanofi and BMS, including the BMS/Sanofi Partnership, committed overt acts in furtherance of the conspiracy as described above.

405. As a result of Defendants' actions, as set forth above, the United States of America has been, and may continue to be, severely damaged.

WHEREFORE, Relator, on its own behalf, the United States Government, and the State Plaintiffs, demands judgment against the above-named Defendants, ordering that:

As to the Federal Claims:

a. Pursuant to 31 U.S.C. § 3729(a), Defendants pay: an amount equal to three times the amount of damages the United States Government has sustained as a result of Defendants' actions, which Relator currently estimates to be in the hundreds of millions of dollars; plus a civil penalty of not less than $6,500 and not more than $11,000 for each violation of 31 U.S.C. § 3729, *et seq.,* or such other penalty as the law may permit and/or require for each violation of other laws which governed Defendants' conduct;

b. Relator be awarded a relator's share of the judgment to the maximum amount provided pursuant to 31 U.S.C. § 3730(d) of the False Claims Act and/or any other applicable provision of law;

c. Relator be awarded all costs and expenses of this action, including attorneys' fees, as provided by 31 U.S.C. § 3730(o) and any other applicable provision of the law; and

4-168(a)(3); 740 Ill. Comp. Stat. 175/3(a)(1)(C); Ind. Code § 5-11-5.5-2(b)(7); Iowa Code § 685.2(1)(c); La. Rev. Stat. Ann. § 46:438.3(D); Mass. Gen. Laws ch. 12 § 5B(a)(3); Mich. Comp. Laws § 400.606(1); Minn. Stat. § 15C.02(a)(3); Mont. Code Ann. § 17-8-403(1)(c); Nev. Rev. Stat. § 357.040(1)(c); N.J. Stat. Ann. § 2A:32C-3(c); N.Y. State Fin. Law § 189(1)(c); N.C. Gen. Stat. § 1-607(a)(3); Okla. Stat. tit. 63, § 5053.1(B)(3); R.I. Gen. Laws § 9-1.1-3(a)(3); Tenn. Code Ann. § 71-5-182(a)(1)(C) and/or Tenn. Code Ann. § 4-18-103(a)(3); Va. Code Ann. § 8.01-216.3(A)(3); Wash. Rev. Code § 74.66.020(1)(c); Wis. Stat. § 20.931(2)(c).

d. Relator on behalf of the United States of America be awarded such other and further relief as the Court may deem to be just and proper.

As to the State Claims:

e. Relator on behalf of each named State Plaintiff be awarded statutory damages in an amount equal to the actual damages sustained by each State as a result of Defendants' actions, as multiplied by the respective FCAs, plus the maximum statutory civil penalty under the respective FCAs for each violation by Defendants within each State, all as provided by the States' respective laws.[183]

g. Relator be awarded its relator's share of any judgment to the maximum amount provided pursuant to the States' respective laws.[184]

h. Relator be awarded all costs and expenses associated with each of the pendent State claims, plus attorney's fees as provided pursuant to the States' respective laws.[185]

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[183] Cal. Gov't Code § 12651; Colo. Rev. Stat. § 25.5-4-305(1); Conn. Gen. Stat. § 17b-301b(b); 6 Del. Code Ann. § 1201; D.C. Code Ann. § 2-308.14; Fla. Stat. Ann. § 68.082; Ga. Code. Ann. § 49-4-168.1(a); 740 Ill. Comp. Stat. § 175/3; Ind. Code § 5-11-5.5-2(b); La. Rev. Stat. Ann. § 46 :438.6(B)(1); Md. Code Ann. Health-Gen. §§ 2-601 – 2-611; Mass. Gen. Laws ch. 12 § 5B; Mich. Comp. Laws § 400.612; Minn. Stat. § 15C.02(a); Mont. Code Ann. § 17-8-403; Nev. Rev. Stat. Ann. § 357.050; N.J. Stat. Ann. § 2A:32C-3; N.Y. Fin. Law § 189.1(g); N.C. Gen Stat. §1-607(a); 63 Okla. Stat. Ann. § 5053.1(B); R.I. Gen. Laws § 9-1.1-3; Tenn. Code Ann. § 71-5-182 and/or Tenn. Code Ann. § 4-18-103(a); Va. Code Ann. § 8.01-216.3; Wash. Rev. Code § 74.66.020; Wis. Stat. § 20.931(3).

[184] Cal. Gov't Code § 12652(g); 6 Del. Code Ann. § 1205; D.C. Code Ann. § 2-308.15; Fla. Stat. Ann. § 68.085; Ga. Code. Ann. § 49-4-168.2(h); 40 Ill. Comp. Stat. § 175/4(d); Ind. Code § 5-11-5.5-6; La. Rev. Stat. Ann. § 46:439.4; Mass. Gen. Laws ch. 12 § 5F; Mich. Comp. Laws § 400.610a; Mont. Code Ann. § 17-8-410; Nev. Rev. Stat. Ann. § 357.210; N.J. Stat. Ann. § 2A:32C-7; N.Y. Fin. Law § 190.6; 63 Okla. Stat. Ann. § 5053.4; R.I. Gen. Laws § 9-1.1-4; Tenn. Code Ann. § 71-5-183(c) and/or Tenn. Code Ann. § 4-18-104(g)(2), (3); Va. Code Ann. § 8.01-216.7; Wash. Rev. Code § 74.66.070; Wis. Stat. § 20.931(11)(a) & (b).

[185] Cal. Gov't Code § 12652(g)(8); 6 Del. Code Ann. § 1205; D.C. Code Ann. § 2-308.15; Fla. Stat. Ann. § 68.086; Ga. Code. Ann. § 49-4-168.2(h); 740 Ill. Comp. Stat. § 175/4(d); Ind. Code § 5-11-5.5-6; La. Rev. Stat. Ann. 46:439.4(C)(1); Mass. Gen. Laws ch. 12 § 5F; Mich. Comp. Laws § 400.610a; Mont. Code Ann. § 17-8-410; Nev. Rev. Stat. Ann. § 357.180; N.J. Stat. Ann. § 2A:32C-7; N.Y. Fin. Law § 190.7; 63 Okla. Stat. Ann. § 5053.4; R.I. Gen. Laws § 9-1.1-4, Tenn. Code Ann. § 71-5-183(c) and/or Tenn. Code Ann. § 4-18-104(g)(8); Va. Code Ann. § 8.01-216.7; Wash. Rev. Code § 74.66.070; Wis. Stat. § 20.931(11)(c).

i. Relator on behalf of the State Plaintiffs be awarded such other and further relief as the Court may deem to be just and proper.

/s/ W. Scott Simmer
W. Scott Simmer (admitted *pro hac vice*)
/s/ Gerald C. Robinson
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Counsel for Plaintiff/Relator
JKJ Partnership 2011 LLP

Dated: February 22, 2017

JURY TRIAL DEMAND

Relator demands a trial by jury of all issues so triable.

/s/ W. Scott Simmer
W. Scott Simmer (admitted *pro hac vice*)
/s/ Gerald C. Robinson
Gerald C. Robinson (NJ Bar No. 028452005)
Andrew M. Miller (admitted *pro hac vice*)
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Counsel for Plaintiff/Relator
JKJ Partnership 2011 LLP

Dated: February 22, 2017

LOCAL CIVIL RULE 11.2 CERTIFICATION

Plaintiff/Relator JKJ Partnership 2011 LLP hereby certifies that, to its knowledge, the matter in controversy in this action is not the subject of any other pending lawsuit, arbitration, or administrative proceeding.

/s/ W. Scott Simmer
W. Scott Simmer (admitted *pro hac vice*)
/s/ Gerald C. Robinson
Gerald C. Robinson (NJ Bar No. 028452005)
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Counsel for Plaintiff/Relator
JKJ Partnership 2011 LLP

Dated: February 22, 2017

CERTIFICATE OF SERVICE

I certify that the foregoing Second Amended Complaint was filed on February 22, 2017, via the District of New Jersey ECF system, which will automatically send a Notice of Electronic Filing (NEF) to all registered participants identified on the NEF. I further certify that on February 22, 2017, I caused paper copies of the Second Amended Complaint to be sent to all parties who are not registered ECF participants.

By: */s/ Gerald C. Robinson*
Gerald C. Robinson, Esq.
SIMMER LAW GROUP, PLLC